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# "FUNCTIONING" PULMONARY NEOPLASMS: I. THE CARCINOID TUMOR; II. THE HEMANGIOPERICYTOMA

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THE initial recognition of the so-called "carcinoid syndrome" by Thorson, Biörck, Björkman, and Waldenström,[1] as a clinicopathologic entity, has expanded the knowledge of functioning tumors to include neoplastic entities not previously believed to possess any endocrine activity. Although the disorder was initially believed to be limited to metastasizing gastrointestinal carcinoid tumors, evidence has accumulated that some malignant and metastasizing bronchial tumors have the same propensity to produce the syndrome of hyperserotonemia. In 1957 a review of 21 cases of bronchial adenoma, encountered and treated at the Cleveland Clinic, was reported.[2] Later, a case of malignant carcinoid diagnosed six months after the removal of a bronchial neoplasm[3] aroused our interest in the possible serotonin-producing properties of these tumors; consequently, we have made a detailed study of the three such tumors encountered since that time.

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An allied problem concerns the nature of the hemangiopericytoma. This type of tumor was originally recognized by Stout and Murray,[4] and a series of cases was reported by McCormack and Gallivan.[5] Korn, Bensch, Liebow, and Castleman,[6] however, have suggested the resemblance of one of these tumors to the "multiple peripheral bronchial adenomas."[7] This stimulated us to make a detailed pathologic and biochemical study of a recent specimen of malignant hemangiopericytoma.

## I. The Carcinoid Tumor

### Report of Cases

**Case 1.** A 49-year-old white man was admitted to the Cleveland Clinic Hospital on January 31, 1960, because of a pulmonary "coin lesion." A routine chest roentgenogram revealed evidence of the lesion that in 1958 was diagnosed as "a small granuloma in the right mid-lung field." The patient was in good health and without a complaint. He underwent a cholecystectomy in 1957; his mother and one brother have diabetes mellitus.

Physical examination showed a well-developed, well-nourished white man in no distress. Oral temperature was 98.6 F.; radial pulse rate was 72 and regular; blood pressure was 140/80 mm. of Hg. The skin was of good color; the cholecystectomy scar was visible over the upper part of the abdomen. The chest was clear, and the heart was normal in size, had a good rhythm, and normal sounds. Cardiac murmurs were absent. The abdomen was scaphoid, and there were no palpable masses or enlarged organs. On a thoracic laminagram there was no evidence of a laminated type of calcification or a halo. A comparison of the current chest roentgenogram with the one in 1958 revealed evidence that the lesion had become sharply demarcated.

The hemoglobin was 16.0 gm. per 100 ml., and the cell volume was 48 ml. The urine specific gravity was 1.013, contained no albumin or sugar, and only an occasional leukocyte. A 5-hydroxyindoleacetic acid study was not done. Purified protein derivative tuberculin, and histoplasmin skin tests were both negative. A bronchoscopic examination revealed no evidence of the lesion, and washings obtained from the right lower lobe and the right main bronchi were free of tumor cells or microorganisms. An electrocardiogram was normal. On February 1, 1960, the patient underwent a right lower lobectomy. The postoperative course was uneventful, and the patient was discharged from the hospital on February 9, 1960. He has had no further pulmonary problems.

**Case 2.** A 54-year-old white man was admitted to the Cleveland Clinic Hospital on February 10, 1960, for investigation and treatment of a lesion in the left lower pulmonary lobe. Evidence of this lesion was discovered in 1956 on a routine chest roentgenogram, but the patient had no further investigation until an intermittent neuromuscular type of chest pain developed and he wondered whether or not there was a relationship between the mass and the pain. Upon admission to the hospital the patient was in good health.

He had had the usual childhood diseases without sequela. In 1921 he underwent a thyroidectomy for "goiter," and in 1956 a colostomy because of "rupture of the bowel." A year later he underwent "repair of the colostomy." Findings from his family history and systemic review were essentially normal.

On physical examination the radial pulse rate was 75; the blood pressure was 198/110 mm. of Hg. General appearance was that of a well-developed, well-nourished, middle-aged, white man with a "slight cyanotic flush to face and extremities," and in no distress. Oral temperature was 98.0 F. A thyroidectomy scar and four abdominal surgical scars were visible. The thorax revealed diminished expansion bilaterally. The breath sounds were diminished throughout the lung fields, but this decrease was more apparent over the apices. There was no dullness or rales or rhonchi. Cardiac murmurs were absent. The abdomen was soft, nontender, and no masses or enlarged organs were palpable. Peripheral arterial pulses were diminished in both lower extremities. A roentgenogram of the chest showed a 2-cm. round, sharply demarcated density in the region of the left mid-lung field. There was evidence of old, healed fractures of the seventh and eighth ribs posteriorly on the left. A vital capacity determination was within the normal range.

Studies of the blood yielded the following values: hemoglobin, 16.4 gm. per 100 ml.; cell volume, 48 ml.; leukocyte count, 5,700 per cubic millimeter, with a normal differential count. The Bromsulphalein test showed 10 per cent of the dye to be retained at 45 minutes. The thymol turbidity was normal. The blood urea was 18 mg. per 100 ml. and a fasting blood sugar concentration was 77 mg. per 100 ml. Electrolyte values were within the normal range. The urine specimen had a specific gravity of 1.022, and it contained no albumin or formed elements. The amount of 5-hydroxyindoleacetic acid in the urine was not determined.

On February 11, 1960, the patient underwent a left lower lobectomy. The operative report stated: "The left lung appears to be quite normal except for the lesion in the left lower lobe which by palpation was centrally located and was quite soft. The hilus is normal except for some minor node involvement which appears to be entirely inflammatory. I was impressed, however, by the moderate increase in pulmonary artery pressure and believe that this patient does have moderate pulmonary hypertension. The etiology of this is not apparent." The postoperative course was relatively uneventful with the exception of a rather severe adynamic ileus that cleared after conservative therapy. The patient was discharged from the hospital on February 25, 1960.

Case 3. A 48-year-old white man was admitted to the Cleveland Clinic Hospital on January 26, 1960, having been referred to us with a tentative diagnosis of bronchogenic carcinoma. About three weeks before that time the patient became ill with "the flu," and because of his slow recovery a chest roentgenogram was made; it disclosed evidence of an infiltrative lesion in the right lung. During the week before admission he improved, and upon arrival had no specific complaint. In 1955 he received antibiotics for "an abscess" in the right side of the chest. Findings from a review of the systems and the family history were essentially normal.

On physical examination he was well-developed, well-nourished, and in no distress. Oral temperature was 100.6 F., radial pulse rate was 80 and regular, and blood pressure was 125/70 mm. of Hg. The skin was of a good color, and there were no lymph node enlargements. The chest was clear according to percussion and auscultation, and examination of the heart disclosed no abnormality. Blood studies showed a hemoglobin content of 13.0 gm. per 100 ml., a cell volume of 40 ml., a leukocyte count of 12,000 per cubic millimeter with a relatively normal differential count. A fasting blood sugar

concentration was 88 gm. per 100 ml. and the blood urea content was 24 mg. per 100 ml. Urinalysis gave the following results: specific gravity 1.020, absence of sugar and albumin, and occasional erythrocytes and leukocytes in the sediments. The amount of 5-hydroxyindoleacetic acid in the urine specimen was not determined.

A bronchoscopic examination on the day of admission disclosed a lesion in the basal segment of the right lower lobe. A culture of bronchial washings produced an alpha hemolytic streptococcus, but neoplastic cells and acid-fast organisms were absent. After the bronchoscopic procedure, chills and fever developed; examination of the chest disclosed a dullness over the right paravertebral basal lung field. Decreased breath sounds and inspiratory rales were present over the same area. A chest roentgenogram revealed an area of infiltrate extending from the right hilus into the right lower lobe, and was thought to be compatible with pneumonitis secondary to obstruction from a neoplasm.

The pneumonic process responded well to treatment with antibiotics, and on February 3, 1960, the patient underwent operation. As a result of the recent exudative process the surgeon was unable to distinguish whether the neoplasm was benign or malignant, and therefore he performed a bilobectomy of the right lower and middle lobes. The patient had an uneventful postoperative course and was discharged from the hospital on February 10, 1960.

*Pathologic findings.* The tumors varied both in their gross and in their microscopic features. In the first patient (case 1) the lesion consisted of a 2.8-cm. red-gray, unobstructing, firm, homogeneous, circumscribed mass. A slight endobronchial protrusion extended into the posterior segment of the lower lobe bronchus. In the second patient (case 2) a 2-cm. gray-purple circumscribed tumor lay beneath the mucosa of the basal segment of the left lower lobe. It similarly expanded into the parenchyma, but no bronchial obstruction was present. In the third patient (case 3) the tumor was a 3.5-cm. by 2-cm. by 2-cm., gray, firm, homogeneous lesion that apparently arose in the posterior basal segment of the right lower lobe, completely obstructed it, and extended slightly into the main bronchus of the right lower lobe *(Fig. 1)*. This extension produced partial blockade of the remaining bronchi to this lobe.

Microscopically, the neoplasm in patient 1 was comprised of uniform small cells so characteristic of the carcinoid of the bronchus *(Fig. 2A)*. The sheets of cells were sharply marginated from blood vessels, and focally contained areas of microcystic formation, which were irregular in shape and size and did not resemble true lumen formation. The microcysts contained a pink granular coagulum. Only at the margins of the tumor was there evidence of cording and small island formation. The individual cells possessed a sparse amount of indistinct pink-staining cytoplasm; the nuclei were uniform, round to oval, and possessed the characteristic chromatin stippling with occasional large masses that might be interpreted as nucleoli, which is so characteristic of these tumors. Mitosis was not apparent.

Fig. 1. Case 3. Photograph of resected right lower lobe. The endobronchial portion is demarcated by retention of bronchial cartilages.

In case 2 the neoplasm had a morphologic pattern similar to that in case 1 *(Fig. 2B),* but the cells were somewhat larger, and there was more cytoplasm present. The cells were sharply marginated from the encompassed blood vessels.

In case 3 the neoplasm had large areas morphologically identical to those in case 1; however, there also were areas where the cells were arranged in cords with greater cell size and more nuclear irregularity *(Fig. 3).* These ribbons of cells contained frequent lumens. They were separated not by dense hyaline connective tissue, but by the microcystic areas that possibly could be degenerative in orgin.

None of these tumors showed evidence of extension beyond their primary locations within the lungs. Regrettably, through a lack of foresight and possibly because of the previous poor results with formalin-fixed bronchial carcinoids, none of the available neoplastic tissue was fixed in formalin, and no report can be given as to the presence or absence of argentophilic granules.

*Biochemical findings.* The presence of serotonin in the tumorous tissue from the first two patients (cases 1 and 2) was established by chromatography and bio-

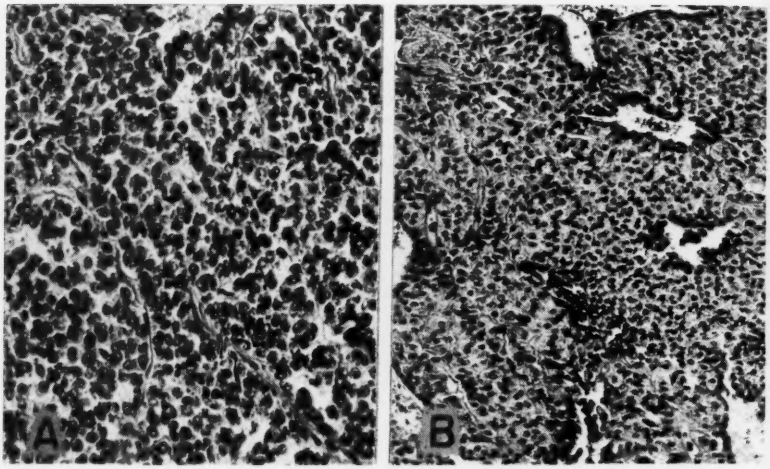


**Fig. 2.** Photomicrographs showing some of the varied carcinoid patterns. A, Case 1, characteristic pattern showing closely packed cells with stippled nuclei. Two microcysts are present. Hematoxylin-eosin stain; magnification X 300. B, Case 2, showing the cells to possess more cytoplasm but the same general type of arrangement. Hematoxylin-eosin stain; magnification X 165.

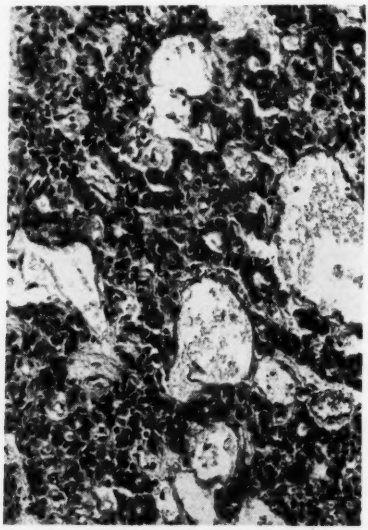

**Fig. 3.** Case 3. Different microscopic patterns are shown in many areas. The microcystic formation is prominent. In addition, acini can be seen in the cords of irregular cells. Hematoxylin-eosin stain; magnification X 160.

assay. Neoplastic tissue was homogenized in acetone, was filtered, and was concentrated to 0.5 ml. in vacuo at 37 C. The concentrate was used for paper chromatography in two solvent systems (A, propanol/ammonia, 7:3; B, butanol/acetic acid/water 4:1:5). A positive Ehrlich-reacting compound with $R_f$* values of 0.48 and 0.54 (in solvents A and B respectively), which were identical with authentic serotonin, was observed. No chromatographic evidence for the presence of serotonin in the neoplastic tissue from the third patient (case 3) was found.

Aqueous dilutions of the concentrate were tested for their oxytocic activity on the isolated rat uterus preparation. The extracts of the neoplastic tissues from patients 1 and 2 had potent activity that could be completely antagonized by the addition of bromolysergic acid to the muscle bath. This provided further proof of the presence of large amounts of serotonin in these tissues. However, the extract of the tumor from patient 3 possessed only weak activity. Estimation of the amount of serotonin present in these tissues was made fluorometrically, using an Aminco-Bowman spectrophotofluorometer;[8] the results are given in *Table 1.*

**Table 1.**—*Identification and estimation of serotonin in bronchial adenoma tissue*

| | Identification | | Serotonin content, micrograms per gram of tumor‡ |
|---|---|---|---|
| Case | Chromatographic* | Biologic† | |
| 1 | + | + | 160 |
| 2 | + | + | 20 |
| 3 | − | ± | 5 |

** Positive Ehrlich-reacting compound with the same $R_f$ as authentic serotonin in two solvent systems.*

*† Oxytocic activity that could be inhibited by bromolysergic acid.*

*‡ Estimated spectrophotofluorometrically.*

## II. The Hemangiopericytoma

### Report of a Case

**Case 4.** A 49-year-old white housewife was first examined at the Cleveland Clinic in April, 1961, because of an asymptomatic nodule evidenced on a chest roentgenogram while the patient was hospitalized for cholecystectomy two months previously. The lesion was not disclosed on a mobile chest roentgenogram two years previously. The

** $R_f$ value is the distance traveled by the compound divided by the distance traveled by the solvent front.*

patient was entirely asymptomatic and had no unusual findings in her medical history. Her mother, a diabetic, had died of carcinoma of the breast.

Physical examination revealed a well-nourished, well-developed white woman in no distress *with no physical abnormalities.* The blood pressure was 160/90 mm. of Hg; height was 62½ inches; weight was 113½ pounds. The heart rate was regular.

A chest roentgenogram delineated evidence of a nodular lesion approximately 2 cm. in diameter in the posterior segment of the right upper pulmonary lobe. The lesion apparently was not calcified; there was no reaction around it. There was no evidence of hilar lymphadenopathy. The blood studies revealed: hemoglobin, 13.2 gm. per 100 ml.; cell volume, 37 ml.; leukocyte count, 10,500 (78 per cent neutrophils, 3 per cent eosinophils, 4 per cent lymphocytes, and 4 per cent monocytes) per cubic millimeter. Urinalysis revealed: specific gravity, 1.020; negative results of sugar and albumin tests; occasional erythrocytes and leukocytes. The patient was hospitalized and underwent a right upper lobectomy; postoperative recovery was uneventful.

*Pathologic findings.* The resected lung contained a 2-cm. tumor near the apex. It was associated with the anterior upper segment of the bronchial tree but did not appear to involve it. On cross section the lesion was faintly pink, firm, homogeneous, and bulged above the surrounding cut surface *(Fig. 4).* Microscopically, the tumor consisted of densely packed, small, spindle cells with hyperchromatic, round to slightly elongated nuclei. The cells were closely applied to thin-walled capillaries, and were arranged in small islands because of the great vascularity of the tumor *(Fig. 5A);* there was an intimate relationship throughout the entire tumor between the blood vessels and the masses of these spindle cells *(Fig. 5B).* Mitotic figures, some bizarre, were encountered in moderate numbers. Necrosis was absent. Fronds of the tumor appeared to extend into the surrounding pulmonary parenchyma. Small blood vessels, both arteries and veins, seemed to contain tumor. Because of the morphologic pattern, the diagnosis was malignant hemangiopericytoma.

*Biochemical studies.* The neoplastic tissue taken for biochemical analysis weighed 2.15 gm. (approximately half the entire tumor). It was homogenized immediately in acetone, was filtered, and then was concentrated. Chromatography did not reveal the presence of serotonin or other indolic compounds. There was, however, chromatographic evidence of the presence of two quaternary compounds that gave positive phosphomolybdic reactions. One of these compounds had the same properties as acetylcholine $R_f$ 0.30 (solvent B). The other compound, $R_f$ 0.90 (solvent B), could not be identified but was not choline $R_f$ 0.25 (solvent B).

Aqueous dilutions of the concentrate were used for bioassay. Oxytocic activity was observed, but since bromolysergic acid only slightly inhibited the smooth-muscle contraction, the major myotrophic component was thought to be something other than serotonin. The contraction, however, could be blocked with atropine (0.1 μg. to the 10-ml. muscle bath) indicating that it was due to acetyl-

**Fig. 4.** Case 4. Resected upper lobe containing the isolated tumor. No statement can be made as to whether the lesion is primary or metastatic; but it is thought to be the former.

choline or an acetylcholine-like compound. The amount present assayed against a standard proved to be equivalent to 10 μg. acetylcholine per gram of neoplastic tissue.

Since the patient had received a small dose of succinylcholine with the premedication, the possibility that the chromatographic and biologic findings might be due to traces of the drug had to be considered. Although unlikely, since a 500-fold concentration in the neoplastic tissue would have been necessary, the possibility was tested in the following way. Two control tumors removed from patients who had received the same type of premedication were extracted and were chromatographed in the same way. There was no evidence of the presence of succinylcholine.

The amount of serotonin present was assayed spectrophotofluorometrically[8] and by bioassay, only that part of the smooth-muscle contraction that could be inhibited by bromolysergic acid being ascribed to the amine. The serotonin content of this neoplasm was 4 μg. per gram of tissue.

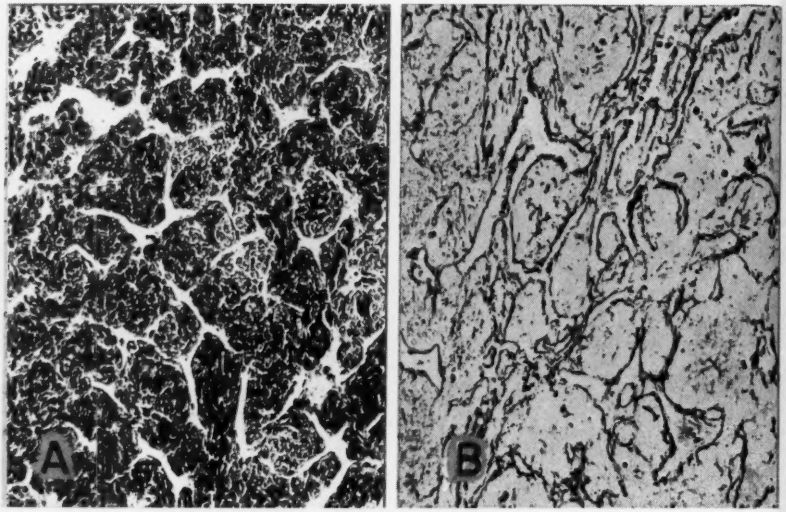


**Fig. 5.** Case 4. A, Photomicrograph showing closely packed cells with their intimate relationship to vascular channels. Hematoxylin-eosin stain; magnification X 160. B, Reticulin stain emphasizes the margins of the vascular channels; magnification X 100.

## Comment

The relationship between certain bronchial neoplasms and the malignant carcinoid syndrome has been recognized by Schneckloth, McIsaac, and Page,[3] and by Sjoerdsma.[9] Others[10,11] even contend that the term "carcinoid tumor" should be used in the diagnosis of all such neoplasms, benign or malignant, within the bronchus. To substantiate this concept, the presence of serotonin in the small, apparently benign tumors had to be established. Our study has demonstrated the presence of significant amounts of serotonin in such small, apparently benign, bronchial tumors. Presumably there are cells within the bronchial mucoscal glands which, although weakly argyrophilic, possess a serotonogenic property. Tumors of these cells, whether benign or malignant, commonly retain this property and consequently should be regarded as "carcinoid tumors."

The results of our biochemical studies of the hemangiopericytoma invite speculation. The presence of a compound that had chromatographic and biologic properties similar to those of acetylcholine, in greater concentration than is found in the central nervous system, would indicate that the tumor had arisen from cells that may have an important physiologic role. If the hemangiopericytoma arises from a specialized cell that occurs as a component of the arteriovenous glomus and produces acetylcholine, this might account for the rapid changes in such arteriovenous shunts in contrast to other capillary action.[12] This straightforward

interpretation of the data is complicated by the presence of another unidentified quaternary compound. Since muscle can produce quaternary compounds, e.g., carnitine, it is not possible at this time to do more than to speculate concerning the physiologic role of the hemangiopericyte.

In conclusion, the correlation of pathologic lesions with the production of physiologically active compounds has proved fruitful in confirming the "carcinoid" nature of some bronchial adenomas, and in arousing speculation in regard to the nature of the hemangiopericyte and its possible role in the regulation of arteriovenous shunts.

## Summary

1. The presence of significant amounts of serotonin in some bronchial adenomas has confirmed the "carcinoid" nature of these neoplasms.

2. The presence of two quaternary compounds, one of which was probably acetylcholine, in a hemangiopericytoma has led to speculation concerning the possible physiologic role of the "glomus cell" in the control of arteriovenous shunts.

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# ATRAUMATIC TECHNIC—THE SINE QUA NON OF OPERATIVE WOUND INFECTION PROPHYLAXIS

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CAN postoperative wound infections be avoided? A positive "yes" in answer to this question would relieve the surgeon of a great burden. It would eliminate physical discomfort and financial hardship for the patient, and it would abolish what has become a new source of litigation in the courts.

The incidence of postoperative wound infection has been reported to be from 1.0 to 37.0 per cent.[1-9] The 2.0 per cent infection rate reported by Meleney and Johnson[7] is used as the standard rate for clean cases. During the past year, in 1,248 consecutive operative procedures performed on the plastic surgery service of the Cleveland Clinic Hospital, only one wound infection occurred, an incidence of about 0.08 per cent. The infection occurred in a patient who had undergone a combined laryngectomy and radical neck procedure.

We believe that postoperative wound infections can be almost completely eliminated by the rigid application of sound surgical principles. The antibiotic era, however, has fostered a relaxation of these principles. The purpose of this paper is to outline the principles that we have found to be successful in the prevention of postoperative wound infection.

## Conditions for Wound Infection

Three factors constitute the cycle that leads to wound infection *(Fig. 1)*; they

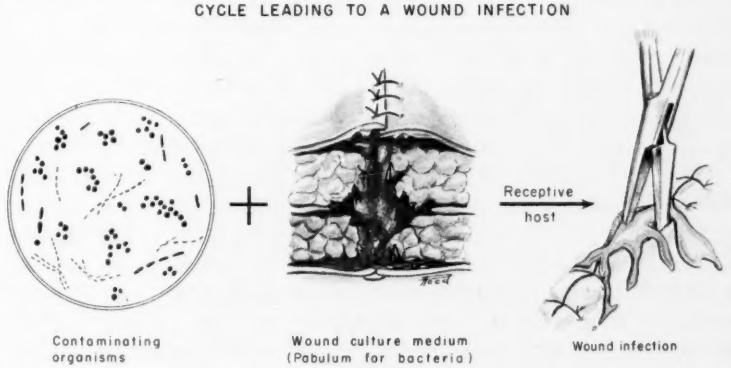


**Fig. 1.** Sketch of cycle leading to a wound infection. A traumatized, poorly closed wound acts as a culture medium in which even a small number of contaminating organisms can multiply and produce a wound infection.

are, in the order of increasing importance: (1) a receptive host, (2) contaminating organisms, and (3) a wound culture medium that acts as pabulum for the bacteria. This cycle can be broken by eliminating any one of the three factors, and a wound infection thereby will be avoided. The important question is "Which factor is the most vulnerable?"

*Receptive host.* With present-day preoperative correction of fluid and electrolyte imbalances, low blood volume, hypoalbuminemia, and avitaminosis, the host is not often the significant factor in the development of wound infections, and for practical purposes can therefore be disregarded.

*Contaminating organisms.* We believe that most wound infections have their genesis in the operating room at the time of surgery. It has been demonstrated[10] that only during the first few postoperative hours is a wound subject to become infected from the environment. It is important to realize that it is impossible to achieve asepsis and sterility, even in the operating room. These terms are only relative. All surgical wounds are contaminated.[9,11] Bacteria have such sources as: the operating room air; the air expired by all operating room personnel and the patient; breaks in the technic during the preparation and draping of the patient, the operation, and the application of the dressings; improperly sterilized equipment; holes in rubber gloves; and dressings. Even if absolute sterility could be achieved insofar as these factors are concerned, the wound still is flooded with organisms as soon as the skin incision is made. Histologically, the skin is not flat, but has millions of microscopic pits leading to skin appendages that are impossible to cleanse of all organisms, and the skin incision immediately permits the organisms to escape into the wound.[11]

*Preparation of the operative site.* The technic of preparing and draping the operative site is the most important variable in controlling the number of organisms that will contaminate a wound. For example, the back and forth motion of scrubbing as shown in *Fig. 2A,* is to be avoided. This method with every stroke drags organisms from a contaminated area into a clean area. The motion should proceed centrifugally, and should extend well beyond the confines of the intended operative procedure, as shown in *Fig. 2B.* We prepare the operative site thoroughly in this fashion for about 10 minutes, using Septisol for the initial scrubbing, followed by benzalkonium chloride aqueous solution. However, the technic and the duration of preparation are far more important than the specific agents used.

Paradoxically, a surgeon may wear two masks, scrub for 10 minutes, put on his gown and gloves, and then operate on a patient whose skin has been prepared for only 30 seconds with a colored antiseptic. Although the preparation of the operative site is far more important than is the preparation of the surgeon, the operative site is frequently prepared by an inexperienced junior resident whose instructions have been inadequate or who lacks close supervision. Fewer wound infections occur when an experienced senior resident prepares and drapes every

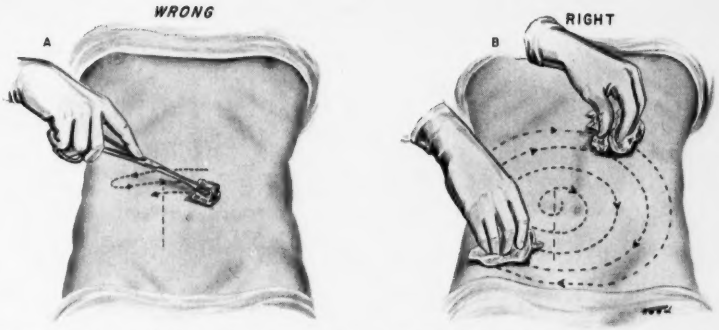


Fig. 2. A, The back and forth technic of preparation of a limited surgical field drags contaminating organisms into the clean field with every stroke. B, The centrifugal method of preparation of a large surgical field is better, aseptic technic.

operative site.

Most of the current papers on wound infections stress the paramount importance of reducing the number of the contaminating organisms. Much emphasis has been placed on such factors as: the use of special masks or two masks, and special gloves, gowns, and sutures; the direction and the amount of traffic in the operating room; the limiting of talking in the operating room; the use of bacteriocidal radiant energy in the operating room; the proper flow of air currents; the carrier status of operating room personnel; the use of a separate room for septic cases; the washing of shoes of all personnel in a bacteriocidal solution; the use of prophylactic antibiotics and special solutions for preparation; sterile technic for postoperative changes of dressings, and the avoidance of a common dressing cart.[1-3,6,8,12-18] We believe that these factors have been given theoretic importance far beyond their practical significance. We do not wish to imply that the contaminating organisms are unimportant. They are important, and we make every effort to keep them at an irreducible minimum; but special devices or schemes do not necessarily accomplish this. In our experience, a thorough scrub, careful preparation and draping of the operative site, and vigilance against breaks in technic, suffice. We should like to stress again that contaminating organisms are present in every wound, and rather than to try to find a way of eliminating all of these organisms, we must find a way to avoid wound infections in spite of them.

*Wound culture medium that acts as pabulum for the bacteria.* The goal should be to decrease the amount of culture medium left in the wound, to the point where the contaminating organisms have no chance to multiply. A healthy, viable wound produced by an atraumatic technic and meticulously closed by accurate approximation of all layers and with obliteration of all potential spaces is the greatest single deterrent to wound infection. It is the sine qua non of uncomplicated,

primary wound healing. Although this was pointed out 40 years ago by Bunnell,[19] this technic has not been stressed in most papers[1-3,6,8,11-13,15,18,20] dealing with wound infections.

We have long observed clinically that a healthy wound can withstand many times the number of contaminating organisms necessary to infect a traumatized wound. This clinical observation was recently corroborated in an experimental study[21] on dogs, in which it was demonstrated that healthy, nontraumatized wounds will heal uneventfully even in the presence of heavy contamination. The converse of this principle was also demonstrated. A granulating wound, such as a burned surface with healthy granulations, is most resistant to infection. There is no magic in the granulations; they are merely indicative that the underlying tissues are healthy. These healthy tissues, then, do not provide a culture medium in which the contaminating organisms can multiply. However, when the granulating surface becomes traumatized, it no longer has the same power to resist infection: a culture medium is established; organisms begin to propagate; and infection may result.

A similar example is that of the child who in the country lacerates his foot. Even though the laceration is made with a highly contaminated object through a contaminated field, and the wound is never sutured, an infection rarely occurs because the wound is healthy. It is only when the dirty wound is traumatized by hemostats, forceps, needles, and sutures that infection is likely to occur.

## Atraumatic Operative Technic

*Handling of wound tissues.* Even with the most gentle handling of tissues, millions of normal cells are killed in every operative procedure. The cut of the sharpest scalpel or scissors destroys many cells. Rough handling of tissues, as shown in *Fig. 3A,* leaves a wound with an ideal culture medium for postoperative infection. The magnitude of this problem becomes clear when one considers the microscopic relationships of tissues. Histologically, tissues are composed of millions of succulent cells held together by a delicate framework of elastic and collagenous fibers, nourished by fragile nerves, lymphatics, and capillaries. Tissues that are torn, pinched, crushed, twisted, pulled, rubbed, scraped, picked, and harshly retracted with a calloused disregard for their histologic structure hardly can be expected to heal uneventfully. Rough handling of tissues produces edema, which impedes normal wound healing. The edema fluid (a) physically separates the tissues that need to unite in healing; (b) causes congestion and sometimes necrosis at the operative site by compressing the venous return; and (c) interferes with tissue metabolism, resulting in an increase in the waste products in the healing tissues.

Constant sponging of living tissue is analogous to sandpapering the conjunctiva. A dry sponge is a harsh abrasive and should be used as such. Repeated sponging

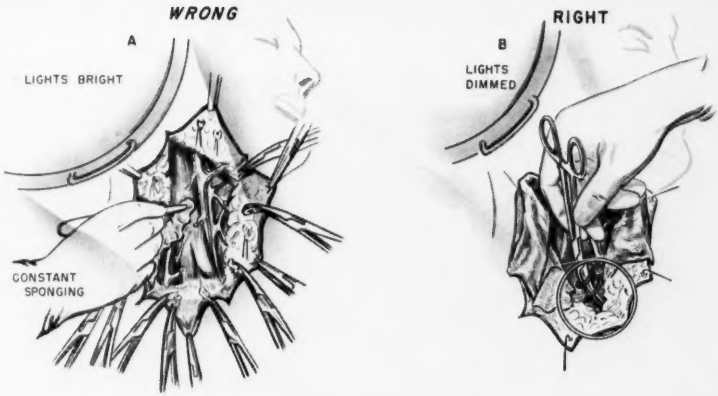


Fig. 3. A, Bright lights, rough handling, constant sponging, drying of exposed tissue, crushing clamps on the skin, too many hemostats with large bites of tissue, and coarse ligatures with long ends, all add to the surgical trauma and increase the possibility of a postoperative wound complication. B, Dimmed lights, gentle technic, moist sponges on exposed tissue, atraumatic hooks on the skin, minimal sponging, few hemostats, and little foreign material increase the likelihood of uneventful healing.

becomes a conditioned reflex, most noticeably exhibited by the operative assistant who immediately after cutting a suture with one hand, sponges with the other hand, whether or not there is blood to remove. Crushing forceps and hemostats should never be used on skin flaps, as they leave areas of devitalized skin. Atraumatic skin hooks should be used to hold the edges of skin flaps during dissection.

Picking up each capillary with a hemostat does more damage than good. The use of too many hemostats, by crushing gross amounts of tissue, produces an excess of suture material and necrotic debris, which acts as a foreign body and increases the wound pabulum. The bleeding from most vessels in the skin and subcutaneous tissues can be controlled by the application of saline packs, at room temperature, to the wound edges, as shown in *Figure 3B.* Other vessels can be individually controlled by picking up the end of the vessel and twisting it several times. Mass ligatures with heavy ties and long ends aid and abet the cycle leading to a wound infection *(Fig. 4A).*

Vessels that bleed persistently must be clamped and must be ligated. They should be picked up with the tip of the hemostat, as shown in *Figure 4B,* and the ligature should be tied directly beneath the hemostat. The finest sutures possible should be used, but it probably makes little difference of what material this tie is made. The ligature should be cut directly on the knot. This technic obviates the inclusion of a large quantity of foreign material in the wound. The unnecessary inclusion of surrounding fat in the hemostat increases the wound culture medium.

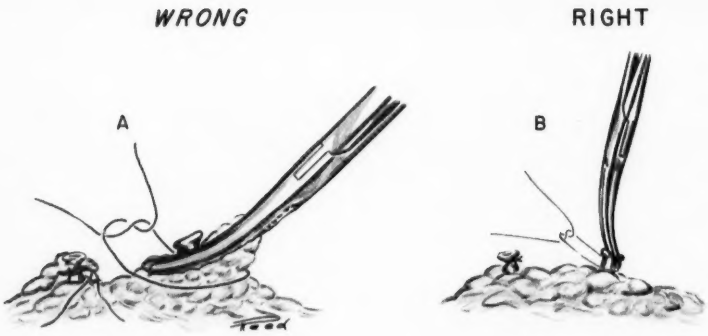


**Fig. 4.** A, Large bites of tissue, coarse ligatures tied too far underneath the hemostat, and long ends on the ligatures leave an excess of necrotic and foreign material in the wound. B, Fine ligatures tied directly beneath the hemostat and cut close to the knot decrease the amount of wound pabulum for the contaminating organisms.

Bright operating room lights contribute significantly to tissue desiccation. Dimming the lights protects the viability of the wound tissues *(Fig. 3B).* The application of saline packs to wound edges also helps to prevent tissue destruction by desiccation. Exposed tissues as those in a neck or a breast operation, should be moistened frequently with saline solution.

*Technic of wound closure.* The surgical technic used in closing the wound is vitally important in the prevention of wound infections. Poor hemostasis, much dead space, devitalized tissue, the presence of foreign bodies, crushing forceps, coarse needles, heavy suture material, coarse ligatures, too many ties with long ends, too much tension on sutures, and overlapping of wound edges, as shown in *Figure 5A,* increase the wound culture medium and therefore the likelihood of wound infection. A careful closure facilitates uneventful, primary healing *(Fig. 5B).*

*Figure 6A* shows a wound that is ripe for infection. A minimal number of contaminating organisms will flourish in the wound pabulum and will produce an infection. *Figure 6B* illustrates an ideal wound, showing the benefits of atraumatic technic, meticulous closure, and the application of a pressure dressing. The tissues are healthy and vital. There is a conspicuous absence of potential spaces, hematoma, excessive suture material, and tissue edema. It is difficult to infect such a wound, because the contaminating organisms can find no culture medium in which to grow.

*Application of the surgical dressing.* The technic of applying the surgical dressing should be considered an important part of the operative procedure. Often it is only a means of hiding the wound from the patient's view. Too frequently the dressing is applied by someone who does not fully understand its purpose

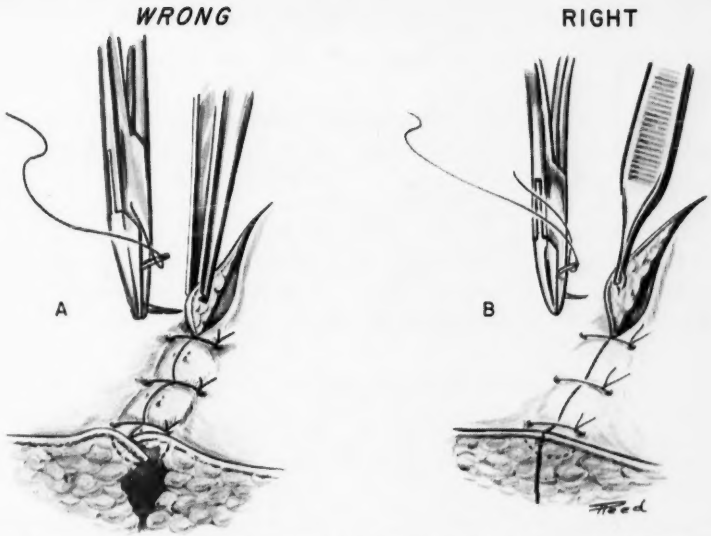


Fig. 5. A, Improper closure with poor hemostasis, crushing forceps, unnecessarily large needles and sutures, overlapping of skin edges, sutures tied too tightly, presence of dead space and tissue edema are conducive to wound infections. B, Proper closure with atraumatic forceps, fine needles and sutures, meticulous approximation of all wound layers, absence of dead space and tissue edema are conducive to uncomplicated healing.

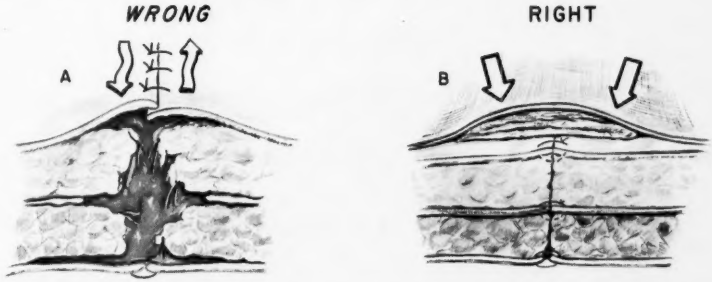


Fig. 6. A, Diagrammatic cross section of a wound that will become infected with a minimal number of contaminating organisms. B, Cross section of a wound atraumatically managed, meticulously closed, and properly dressed with a pressure dressing. Such a wound is most resistant to even heavy contamination.

or usefulness. A properly applied pressure dressing serves many functions that promote uneventful healing: immobility of wound edges; hemostasis; abolition of potential spaces, tissue edema, hematoma formation, and serum collections; and exclusion of the wound from the outside environment.

## Summary and Conclusions

1. Postoperative wound infections have been reported to range in occurrence from 1.0 to 37.0 per cent.

2. During the past year 1,248 operative procedures were performed on the plastic surgery service at the Cleveland Clinic Hospital, and only one wound infection occurred, an incidence rate of about 0.08 per cent.

3. Occurrence of a wound infection has three requisites: (1) a receptive host, (2) the presence of contaminating organisms, and (3) a wound culture medium.

4. The application of sound surgical principles with particular emphasis on atraumatic technic, is stressed as the sine qua non of operative wound infection prophylaxis. Special devices and procedures are not necessary.

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# PITFALLS IN THE SURGICAL CLOSURE OF ATRIAL SEPTAL DEFECT

## Based on Experience with One Hundred and Fifteen Cases

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SURGICAL closure of atrial septal defects was attempted first by external technics wherein the redundant wall of the right atrium was imbricated against the septal rim of the defect.[1-4] The surgeon relied upon his index finger for orientation—that, and a preconceived mental picture of how a characteristic atrial defect should lie in relation to other structures. The imbrication technics reached their ultimate with the ingenious Sondergaard[5] approach wherein the dissection was carried on within the plane of the septum itself. In effect, this technic resulted in a purse-string closure of the centrally located ostium secundum defect.

The limitations of the imbrication methods for closing septal defects at the atrial level soon became apparent. Atrial defects even in their simplest form are not standard in size and location. There is considerable variation in related anatomic features, and the need for a direct open approach was soon realized. The well technic of Gross[4] was the first practical breakthrough in this direction.[6] With this technic a surgeon could not see within the depths of the operative field, but his range of "digital visualization" and his surgical maneuverability were greatly increased *(Fig. 1)*.

There is no doubt that by application of these earlier methods many patients were treated effectively and were relieved of their interatrial shunts. Unfortunately, some patients were not improved and others were made worse, as the surgeon could not cope with complex underlying problems that were beyond limitations imposed by these technics. In the light of present-day knowledge, the early methods briefly described above must be considered obsolete.

### Direct Closure of Atrial Septal Defects

The surgical treatment of atrial septal defects today is accomplished under direct vision. The open approach is performed with hypothermia alone or with some form of extracorporeal circulation. It would appear that this former method is losing favor. Increasing experience with the unhurried approach that is provided by adequate extracorporeal circulation has taught the surgeon invaluable lessons. Most important of these are the multiplicity of facets associated with septal defects at the atrial level, and the wide range of potential surgical errors. Whereas accurate physiologic and anatomic appraisal of atrial septal defects can be accomplished in

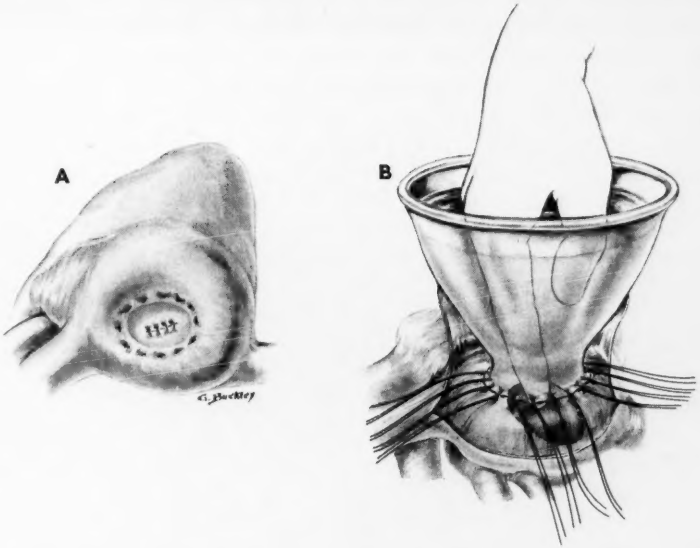


**Fig. 1.** A, Illustrates the principle of the external imbrication technic for closure of ostium secundum defects in the atrial septum. This is the basic method described by Bailey and associates,[1] modified by Lam,[3] and others. This method is accomplished by intraatrial digital palpation and external application of sutures. B, Illustrates the principle of the Gross[4] well technic. Although the surgeon was not able to visualize the surgical field, the basic approach must be considered a precursor of the "open-heart" methods.

the cardiovascular laboratory, the ultimate appraisal of anatomic details must take place within the operating room. Defects of the atrial septum provide the simplest and the most common of all intracardiac shunts. Hence, it is the responsibility of all interested surgeons to combine efforts that will make operations upon interatrial defects safe, simple, and relatively free of complication.

## Surgical Pitfalls

Postoperative bleeding, inadequate pulmonary ventilation, infection, acidosis, air embolus, and cardiac arrhythmia are potential complications that may follow any type of cardiac surgery. It would serve little purpose to discuss management of these specific complications, as they are well understood by all cardiac surgeons. There is an increasing number of new surgical teams that are entering the expanding field of open-heart surgery. These teams consist of well-trained surgeons who have a clear concept of the physiologic and the anatomic problems that will be encountered. Dissemination of specific detailed information that would enable the less experienced surgical groups to avoid tragic accidents that have occurred

in the development of open-heart surgery is an obligation of the surgeons who are established in this field *(Fig. 2)*. A detailed description of potential pitfalls that may be encountered in a closure of a relatively simple atrial septal defect may be of value. The observations to be described are based upon experience and


**Fig. 2.** Diagrammatic representation of the surgical field in the closure of an ostium secundum defect utilizing extracorporeal circulation. Surgical closure of this common form of atrial septal defect does not require elective cardiac arrest. The systemic venous return to the heart is diverted to the pump-oxygenator by two caval cannulae. The complete bypass is assured by the use of tourniquets that compress the venae cavae around the indwelling venous cannulae. With this technic the only blood return to the heart is that which enters from the coronary circulation and the bronchial vessels whose drainage enters the left atrium. With the patient in a supine position, right side slightly elevated, the left heart maintains a dependent position. A sterile sucker is used to keep the right atrium relatively dry. The blood level is never lowered below the plane of the atrial septum itself; in this way the hazard of air embolus is avoided. With this exposure and with the unlimited time afforded by good extracorporeal circulation, the surgeon may inspect his field with meticulous care and identify his landmarks with a certainty: the tricuspid valve, the coronary sinus, and unsuspected anomalous drainage of the pulmonary veins can be visualized. Although the majority of published illustrations suggest that the ostium secundum defect presents a standard appearance, this is by no means true. There may be considerable variation in size, location, and character of the membranous tissue that comprises the septal remnant.

on surgical lessons that have attended 115 open-heart operations for the treatment of ostium secundum defects. The complicated problems related to the ostium primum type of defect and atrioventricular communis will not be discussed in this paper.

1. *Inadequate closure.* Most ostium secundum defects visualized at surgery are related to faulty development of the foramen ovale. The surgeon usually finds a remnant of valve flap on the inferior aspect of the defect itself. This meniscus of tissue may be exceedingly thin and almost avascular in character; it, too, may contain fenestrations that are overlooked when the operation is performed in haste. A continuous suture that utilizes this thin partition as the inferior segment of the septum may not be of lasting support. Subsequent fenestration may result, and may produce a virtual reopening of the entire defect. It is worthy of emphasis that the surgeon must be permitted an unhurried appraisal of the atrial septum and its related structures. Although the initial surgical closure may easily be accomplished by a continuous suture, to insure complete interruption of the atrial shunt, meticulous reinforcement by carefully placed interrupted single or mattress stitches is necessary *(Fig. 3).*

It would seem self-evident that a meticulous, well-conceived closure of a simple atrial septal defect would be the only acceptable operation for this common lesion. It is unfortunate that this concept is not in general acceptance; perhaps the basic simplicity of the anatomic defect itself has encouraged operative technics that are almost slapdash in character.

2. *Prosthetic repair.* Direct efforts to close atrial septal defects by means of the Gross well technic frequently utilized a prosthetic patch. The vogue for patch closure of ostium secundum defects carried over into the period of open-heart surgery that utilized extracorporeal circulation. It is safe to say that many types of prosthetic devices were utilized in the reconstruction of the atrial septum before the ultimate fate of these foreign bodies had been ascertained. Subsequent experimental work as described by Kolff and his co-workers,[7] illustrates the encapsulation of prosthetic patches by various blood elements; this may begin by an initial clot that is subsequently replaced by heavy fibrous tissue, and occasionally by calcification. There is no question that the majority of prosthetic patches when properly positioned serve a useful and permanent purpose; however, results in a significant number of cases have demonstrated that the prosthetic patch on occasion may prove to be a poorly tolerated foreign body that becomes a liability to the host.

On the basis of our experience here, it would appear that prosthetic repair of an uncomplicated secundum defect is indicated rarely. The tissues of the atrial septum, which surround even the larger defects, are rather elastic and under little stress when compared to those at the ventricular septal level. Therefore, direct suture closure can be accomplished in the large majority of patients. It is not to be construed that prosthetic repairs of atrial septal defects are never indicated or

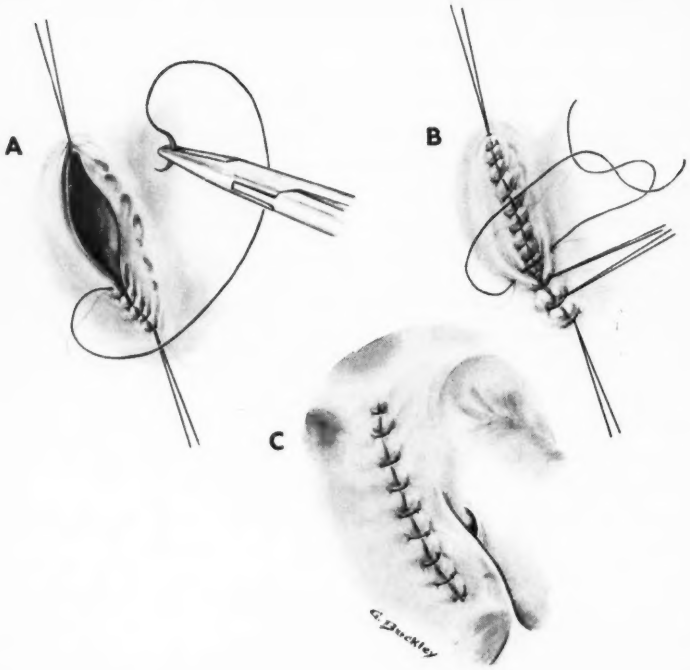


**Fig. 3.** Surgical closure of ostium secundum defect is accomplished by direct suture in the majority of operations. The routine use of a plastic prosthesis is to be condemned. Direct inspection of the defect permits the surgeon to select the plane of closure. A, Shows how this plane is further developed by the placement of interrupted sutures at each end of the plane of closure. Initial closure may then be accomplished by a direct continuous silk suture. As mentioned in the text, the ostium secundum defect presents in most instances a meniscus of thin fibrous tissue that may represent the valve flap of the foramen ovale. This tissue flap may be papyraceous in character and prone to subsequent fenestration when subjected to the stress of cardiac motion. For this reason it is good practice to utilize a series of interrupted sutures, B, to reinforce the original closure. This second line of closure will reinforce the original suture line when the needle bites are brought through selected areas in the septum where tissue substance is increased. This is not difficult to accomplish after initial closure of the shunt. Again, it must be emphasized that the surgeon must have the security of unlimited time as provided by extracorporeal circulation, if this method is to be employed. C, Shows the completed surgical closure of an ostium secundum defect.

that all are doomed to ultimate failure. There will always be instances where success cannot be achieved without the use of prosthetic material, particularly when the defects are extremely large and are associated with anomalous pulmonary venous return. The fact remains that the prostheses are foreign bodies, and their presence within the heart may constitute a serious liability, particularly in the presence of

infection. For this reason, the author believes that prosthetic devices should be used rarely in the surgical treatment of ostium secundum defects.

3. *Intracardiac conduction.* In our experience, permanent heart block has never occurred in the surgical closure of ostium secundum defect. Transient cardiac arrhythmias are common occurrences during the actual operative procedure, and it is likely that they are stimulated by the sterile aspirator and the surgical instruments.

In the experimental animal, complete heart block may be produced by placing sutures through large sections of the lower posterior aspect of the atrial septum close to the ventricular cushion; in the human, the utilization of massive suture bites is not indicated. In those defects that are low and close to the tricuspid valve it has been our practice to use simple interrupted sutures placed with meticulous care, and every effort is made to avoid the producing of necrosis of local tissue, which might reflect damage to the conductive tissue. In the ostium secundum defect there will always be some septal remnant above the level of the tricuspid valve which will be safe to use for supporting suture material.

4. *Anomalous venous drainage.* Atrial septal defects may be associated with anomalous pulmonary venous return. This situation usually is recognized after preoperative catheterization study. When the orifice of the pulmonary vein is close to the septal aspect of the defect and a large shunt volume is present, the diagnosis may not be obvious. When anomalous venous drainage of the right lung is present and not recognized, the surgeon may close the defect without regard for the misplaced venous orifice. This error is most likely to occur when the surgeon is distracted by the need for haste or by inadequate support from anesthesia.

This technical error is best avoided by inspection of the pulmonary veins of the right lung before the atrial incision is made. It is good practice to make a routine inspection of the superior vena cava above the level of the azygous vein, as unexpected communications between the vena cava and the venous drainage of the upper lobe may exist. Routine establishment of the presence or the absence of anomalous venous return to the right atrium should be done after the right atrium is entered and the initial surgical inspection has been made.

When the venous drainage of the right upper lobe enters the superior cava above the level of the azygous vein, it has been our practice to sacrifice the entire lobe rather than to attempt to transpose the vein itself. When the venous return from the right lung enters the right atrium in the region of the septal plane, the problem is best handled by extending the septal plane to the right of the venous orifices; under these circumstances the use of a prosthetic patch may be mandatory.[7]

5. *Diversion of inferior vena caval return.* Clinical experience has demonstrated an occasional variation in the internal topography of the inferior vena caval orifice. The junction of the right atrium and the orifice of the inferior vena cava may, on direct inspection, resemble the open end of a funnel. Sometimes, however, a

flap of thin fibrous tissue exists in the form of a peculiar valve flap that takes a circumferential origin from the vena caval orifice itself. This membranous structure seems to be variable as to its exact point of origin, its size, and even as to its presence or absence. Nevertheless, it can exist and, in the presence of a large low-lying atrial septal defect, may constitute a surgical booby trap.

An open-heart operation for atrial septal defect requires occlusion of the inferior vena cava by clamp or by tourniquet.[8] This alters greatly the appearance of the vena caval orifice as it is inspected from within the atrial chamber itself. Whereas the inferior vena cava normally is a large tubular structure, it now appears as a wrinkled or fluted orifice comprised of thin flaccid tissue. It is important that the surgeon keeps this morphologic point in mind, particularly when dealing with a low-lying septal defect whose lower margin lies close to the superior vena caval orifice *(Fig. 4)*.

The importance of the peculiar valve flap arising from the inferior vena caval orifice, and the fact that there is considerable anatomic distortion associated with vena caval occlusion were not appreciated by the authors until the combination of the two conditions led to an unfortunate surgical accident. While a large low-lying ostium secundum defect was being closed under direct vision, the inferior vena caval flap was erroneously identified as part of the inferior septal rim of the defect itself, and it was incorporated in the suture line when the major part of the defect was being closed. The fact that large vena caval cannulae had been used and were in proper position, only contributed to the false sense of security. It became apparent soon after the operation that a serious error had been made, and that a significant amount of systemic venous return to the heart was being diverted into the left atrium. It is indeed fortunate that the patient survived after a stormy period of convalescence, and that reoperation was possible. At the second operative procedure it was apparent that the entire inferior vena caval return was entering the left atrium. Apparently the development of healing fibrosis had compounded the original surgical error.

Accidental diversion of the inferior vena caval flow to the left atrium is by no means a rare accident. For understandable reasons, this error has not appeared prominently in surgical literature; however, by personal communications we have become aware of a number of instances in which this accident has occurred.[9] In every instance it has been the inferior vena cava that has been involved; diversion has been virtually total, and the patients have survived only after considerable postoperative difficulty.

It would seem that prevention of this surgical accident would depend first of all upon the surgeon's knowledge that the possibility for such an accident exists. It is the authors' policy when dealing with low-lying atrial septal defects to make a careful identification of related anatomic structures before making any effort to effect closure. The orifice of the coronary sinus, the vena caval orifice itself, the

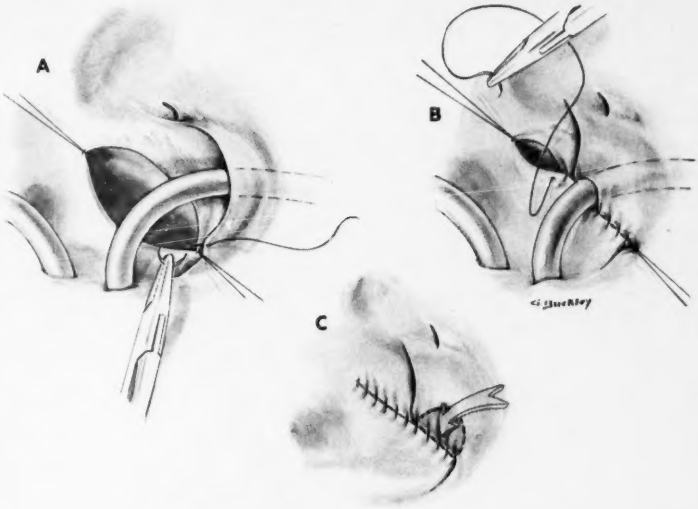


Fig. 4. Diversion of the inferior vena cava to the left atrium constitutes one of the most serious pitfalls in the surgical closure of atrial septal defect. As mentioned in the text, the authors assumed that the presence of vena caval cannulae would prevent this surgical mishap. Experience has shown that the only protection against this accident is the knowledge that it can occur and perfect orientation throughout the operative procedure. A, Illustrates how atrial defect of the ostium secundum type is usually closed on an oblique plane. In the presence of a well-developed thebesian valve that projects from the orifice of the inferior vena cava, the surgeon may erroneously identify it as the inferior aspect of the rim of the defect. This error has been made by experienced surgeons and is understandable when there is a large flow of blood across the defect from the left atrium and this is compounded by the motion of the heart plus the need for completion of the operation within a specified time. B, Illustrates one method in which the caval flap is incorporated in the surgical closure of a low-lying ostium secundum defect. This accident is prone to happen in operations performed under hypothermic technics where time is an essential factor and vena caval cannulations are not required. Partial or complete diversion of the inferior vena caval return to the left atrium will result when the inferior vena caval flap is incorporated by mistake into the surgical closure of the low-lying septal defect. C, Illustrates the completed erroneous repair after removal of the inferior vena caval cannula. The vena cava drains completely into the left atrium.

presence or absence of a vena caval flap, and the position of a septal rim in relation to the inferior pulmonary vein are all verified; additional protection is afforded by the utilization of interrupted silk sutures to initiate the defect closure at its posteroinferior aspect. In some instances it is our practice to initiate the sutures from outside the atrial wall immediately above the junction between the posterior aspect of the inferior vena cava and the right atrium. These sutures are tied externally. The most important safeguard, however, is the practice of releasing inferior vena caval occlusion immediately after septal closure has been accomplished. If the vena caval orifice is in normal relatio : to the atrial septum, there

will be a cascade of unsaturated blood into the right atrium—if this does not occur, complete revision of surgical closure is in order. It has been suggested by Scannell[9] that retrograde cannulation of the inferior vena cava by way of the femoral vein may be an additional safeguard to avoid the serious accident of inferior vena caval diversion to the left atrium.

## Summary and Conclusions

Surgical closure of atrial septal defects is best accomplished under direct vision, and utilizing extracorporeal circulation. The ostium secundum type of atrial septal defect is the simplest intracardiac shunt to repair, but it is well for the surgeon to recall the certain pitfalls that may be encountered.

Any operation within the heart that utilizes extracorporeal circulation or hypothermia alone may be subject to complications associated with hemorrhage, infection, metabolic acidosis, air embolus, and cardiac arrhythmia. For the most part these complications are well understood and are avoidable.

Experience in 115 operations for simple atrial septal defects has convinced us that the overwhelming majority may be closed by a direct suture technic. In all probability, prosthetic closures should not be used unless loss of septal substance is of such magnitude that direct closure is impossible, or the surgeon is confronted with anomalous pulmonary venous return. Under these circumstances prosthetic closure is indicated.

Perhaps the most serious and least publicized surgical error associated with the closure of atrial septal defect is inadvertent diversion of the inferior vena caval return to the left atrium. This may be avoided if the surgeon is aware that the possibility exists and he utilizes routine simple precautions.

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will be a cascade of unsaturated blood into the right atrium—if this does not occur, complete revision of surgical closure is in order. It has been suggested by Scannell[9] that retrograde cannulation of the inferior vena cava by way of the femoral vein may be an additional safeguard to avoid the serious accident of inferior vena caval diversion to the left atrium.

## Summary and Conclusions

Surgical closure of atrial septal defects is best accomplished under direct vision, and utilizing extracorporeal circulation. The ostium secundum type of atrial septal defect is the simplest intracardiac shunt to repair, but it is well for the surgeon to recall the certain pitfalls that may be encountered.

Any operation within the heart that utilizes extracorporeal circulation or hypothermia alone may be subject to complications associated with hemorrhage, infection, metabolic acidosis, air embolus, and cardiac arrhythmia. For the most part these complications are well understood and are avoidable.

Experience in 115 operations for simple atrial septal defects has convinced us that the overwhelming majority may be closed by a direct suture technic. In all probability, prosthetic closures should not be used unless loss of septal substance is of such magnitude that direct closure is impossible, or the surgeon is confronted with anomalous pulmonary venous return. Under these circumstances prosthetic closure is indicated.

Perhaps the most serious and least publicized surgical error associated with the closure of atrial septal defect is inadvertent diversion of the inferior vena caval return to the left atrium. This may be avoided if the surgeon is aware that the possibility exists and he utilizes routine simple precautions.

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# EXPERIENCE WITH THIRTEEN CASES OF RESECTION OF ANEURYSMS OF THE DESCENDING THORACIC AORTA

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THE fifteen years since the end of World War II have seen an unprecedented extension of knowledge and development of technics in virtually all fields of surgery. In no area has this development been more dramatic than in that of surgery of the great vessels. In this brief time, for all practical purposes, is encompassed the entire history of aortic surgery as we know it today. This paper discusses surgical experience with aneurysms in the descending thoracic aorta. Ten years ago, such aneurysms were hopeless problems and eventually were fatal. Now, definitive surgical cure is possible.

Many surgeons have made significant contributions to this field; however, the major credit for the technics described in this paper must go solely to the surgical group in Houston, Texas, under the leadership of Dr. Michael E. DeBakey. Each important phase of the technics described has been reported in every essential detail by this group.[1,2]

Surgical resection for coarctation of the aorta, a procedure that is now more than 15 years of age, first established the feasibility of anastomotic procedures on this vessel; but resection, with either direct anastomosis or insertion of a graft, for coarctation differs from resection for aneurysm in one basic condition—the patient with coarctation is born with his aorta "clamped," and with excellent collaterals around the obstruction. He thus can tolerate additional clamping of this area of the aorta for unhurried anastomotic procedures without significant hazard of ischemic problems to the spinal cord or to other vital organs distally distributed in the arterial tree. The patient with an aneurysm does not have comparable collaterals, and hence cannot tolerate protracted interruption of aortic flow. In the infancy of the surgery for aneurysm, this problem was partially overcome by the use of hypothermia, which significantly increases tissue tolerance to anoxia; but 'racing the clock' is apt to be hard for the surgeon as well as the patient. Sudden clamping of the thoracic aorta also imposes an abrupt increase in work on the heart, which may not be well tolerated if significant heart disease is present.

The current means of defeating the time problem are shunt procedures to bypass a portion of the circulating blood around the obstruction during the operative procedure. Some of these shunts are taken down at the completion of the operative procedure; in other instances the shunts are left in situ to function as the new aortic channel after the aneurysm has been resected and the remaining aortic ends have been closed.

Our experience at the Cleveland Clinic Hospital is confined to one particular type of shunt with which we are eminently satisfied, and with which we have had no technical difficulties. This shunt was developed by Doctor DeBakey and his colleagues.[1,2] The shunt runs from the left atrium to a common femoral artery. The left atrium contains oxygenated blood; no oxygenator is necessary. A simple pump is needed to maintain a flow of blood from the low-pressure left atrium into the peripheral arterial circuit.

Technically, we have found it simplest to insert a plastic cannula retrograde into a common femoral artery through a small incision in the groin before commencing the operative procedure. This necessitates heparinizing the blood of the patient at this time. As soon as the chest is opened, a pericardial incision is made to expose the left atrial appendix, and a similar cannula is inserted into the left atrium through a purse-string suture around the tip of its appendix. These cannulae are then connected through a pump, and all is in readiness to perfuse the lower half of the body should circumstances dictate rapid occlusion of the aorta proximal to the aneurysm *(Fig. 1)*.

We have confirmed the experience of others[2] that a flow of 20 ml. per kilogram of body weight per minute through this shunt is adequate, and have seen no evidence of ischemic changes to the nervous system or the kidneys. The operator of the pump has some control over the patient's blood pressure, proximal to the aortic clamp, by varying the pump speed and thus controlling the volume of blood that is "bled-off" from the heart. In our experience, a flow of 30 ml. per kilogram of body weight will lower the arm blood pressure below normal. This shunt is out of the way of the operative field and is readily taken down when the need for it has passed. The only possible objection to it is that the operation must be performed on a heparinized patient, though this has not proved to be a technically important drawback. We discontinue the shunt flow and neutralize the heparin with protamine immediately upon re-establishing aortic continuity with a graft.

Aneurysms involving the ascending aorta and the take-off of the major aortic branches in the arch pose a perfusion problem and a technical problem that are much more complicated than those involving aneurysms occurring distally to the take-off of the left common carotid artery. The shunt system described above allows the patient's normal circulation to perfuse the brain when the aorta is clamped to the left common carotid artery origin. Any aortic aneurysm proximal to the left subclavian artery, unless it is a lateral saccular aneurysm that can be treated by simple aneurysmorrhaphy after cross-clamping its base, necessitates the use of additional shunts to the carotid arteries with or without the use of a pump and an oxygenator, and total cardiac bypass. After the perfusion problems the excision and the graft replacement also may be extremely complicated.

Surgical mortality in such cases is high, and successfully treated cases con-

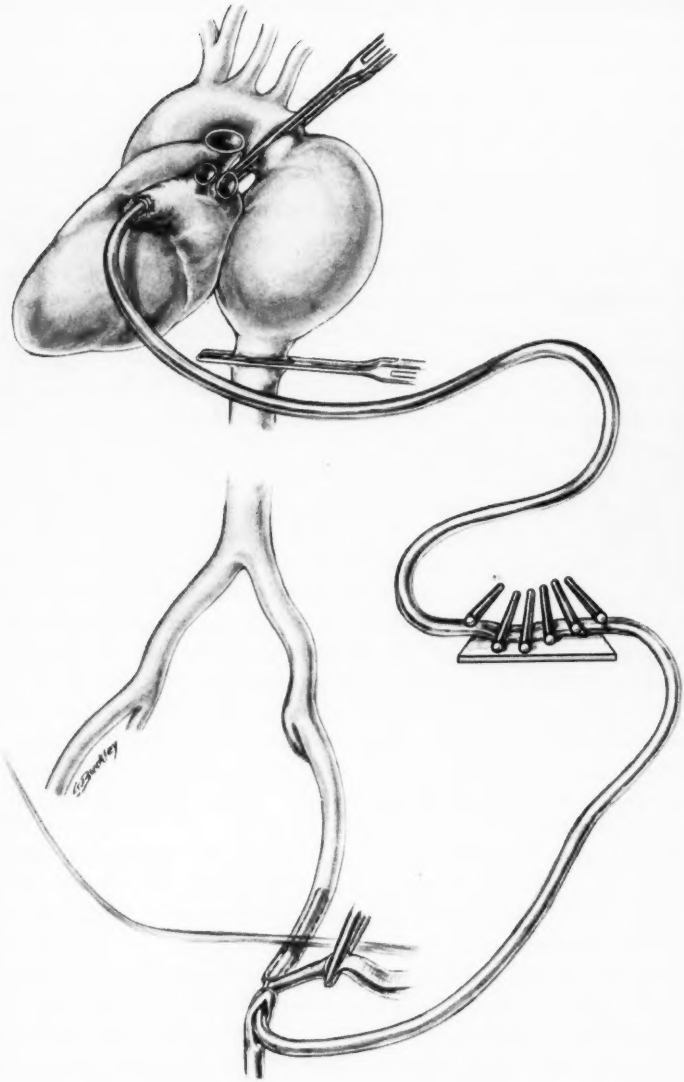

**Fig. 1.** Graphic demonstration of the left-sided shunt bypass used in the cases described. It is readily seen how oxygenated blood withdrawn from the left atrium is pumped into the distal arterial tree to make indefinite periods of aortic occlusion tolerable.

stitute only isolated case reports.[3-9] As opposed to the gratifying salvage that may be anticipated like those discussed below, the factors mitigating against success in an aortic arch aneurysm must be carefully evaluated before accepting an individual case for surgery. I should like to make a plea, however, for exceedingly careful delineation of the extent of almost every aortic aneurysm, as frequently an aneurysm that appears to fill the mediastinum and almost certainly to involve the arch, when it is delineated by contrast medium study, is found in actuality to arise in a favorable location distally to the origin of the cerebral circulation *(Fig. 2)*.

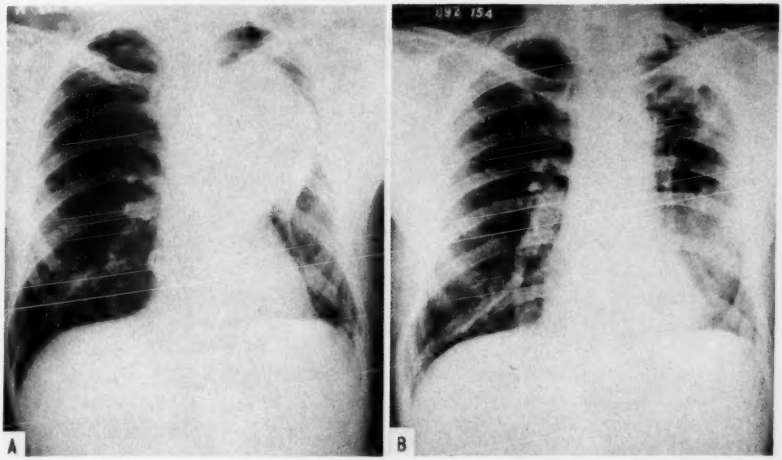


Fig. 2. A, Preoperative, and B, postoperative roentgenograms of a 52-year-old man who had severe respiratory obstruction. Bronchoscopically the terminal tracheal region was greatly narrowed and distorted. Selective cineangiographic visualization of the aortic arch in this patient proved the aneurysm to arise distally to the left subclavian artery, and therefore it was eminently suitable for resection. The resection was complicated by distortion of the left pulmonary hilar structures over the aneurysmal wall; the left main pulmonary artery was traumatized, but could be reconstructed.

## Surgical Experience

Within the past four years the author has had personal experience with 13 patients *(Table 1)* in whom the left atrial-femoral arterial shunt was utilized exactly as described. In each patient the shunt was prepared for function as the initial stage of the operative procedure, and in every patient its use proved necessary. To date no patient was misjudged insofar as the indications for this shunt are concerned. That is to say, no patient underwent exploration without the shunt's being available and found to be necessary, nor has the shunt been set up and not been needed. If one maintains a high index of suspicion of aneurysm in the differential diagnosis of mediastinal masses, he will avoid exploration of unsuspected aneurysms *(Fig. 3)*.

**Fig. 3.** This venous angiocardiographic film demonstrates an asymptomatic descending aortic aneurysm. On a conventional film this shadow appeared as evidence of an undiagnosed posterior mediastinal mass. In case of doubt, studies of this kind are valuable, in order to avoid exploring an undiagnosed aneurysm.

No aneurysm in the thoracic aorta distal to the left common carotid artery has been encountered which did not require aortic occlusion and the use of a shunt, although such aneurysms do occur.

From histopathologic evidence, 10 of the 13 aneurysms are considered to have been of arteriosclerotic origin. Of the 10, two were dissecting aneurysms sufficiently localized so that the entire dissection was resected in each case. An additional two patients of the group had positive serologic tests and fairly conclusive evidence of syphilis; however, the histopathologic findings were solely those of arteriosclerosis. Of the other three aneurysms, one was syphilitic *(Fig. 4),* and two were posttraumatic in origin. One posttraumatic aneurysm was related to a remote history (10 years) of chest trauma in an automobile accident, the significance of which was fully appreciated only when the aortic specimen was examined and showed a smooth circumferential discontinuity of the aortic intima a short distance distal to the left subclavian artery take-off. This is the typical location for such aortic aneurysms.[10]

Of the 13 patients, 10 survived to leave the hospital. Of these 10 patients,

three subsequently died. One died three years after surgery; a chain of aneurysms involving the entire aorta and femoral arterial system had developed. His death was associated with massive hematemesis, presumably representing rupture of an aneurysm into the gastrointestinal tract. One death after the patient was discharged from the hospital was associated with upper gastrointestinal hemorrhage two months after operation. An autopsy at another hospital is said to have shown the graft to be completely intact and that the bleeding was unrelated to it, but was associated with a hiatus hernia. We had known of the presence of a hiatus hernia; however, it was believed at the time of his aortic surgery to be unwise to increase the scope of the operation. One late death occurred eight weeks after operation; the patient was an extremely cachectic 69-year-old man who was readmitted to the hospital because of deficient wound healing and inanition. A tracheotomy wound was larger than when the tube had been removed six weeks previously. An empyema developed in the operative field, and at postmortem, after exsanguination via the site of empyema drainage, the empyema was found to extend to the graft and to the localized leak at the distal anastomosis. We do not consider this a case of primary graft failure.

There were three postoperative hospital deaths in this series of patients. One death occurred eight hours after operation in a 33-year-old man, the youngest in the group, who had a posttraumatic aneurysm. It became apparent that he was having massive hemorrhage into the operated left hemithorax. He was returned to the operating room and the chest was rapidly reopened. The hemithorax was full of blood. It was impossible to resuscitate the circulation, which failed coincident with reopening the chest. We were unable to demonstrate the point of this bleeding satisfactorily either at the time of the reoperation or at the postmortem. The aortic suture lines were intact. The second death in the hospital was due to an acute enteritis, and occurred one week after operation. The patient was treated intensively with novobiocin;* and at postmortem no staphylococci could be cultured, but presumably they were the infecting organisms. The third death in the hospital occurred in an abrupt fashion approximately one-half hour after the completion of the operation. The patient was a 68-year-old woman with a dissecting aneurysm *(Fig. 5)*. During resuscitative efforts a left hemothorax was encountered. At postmortem she was found to have a new and separate acute full-thickness dissection approximately 1 cm. above the proximal anastomosis. Probably her degenerative (atherosclerotic) aortic disease did not tolerate the occlusive clamp that lay at approximately this level during the operative procedure.

In addition to these three fatal complications, three other major postoperative complications occurred which were successfully overcome. In one patient, approximately 10 days postoperatively, roentgen evidence of a localized hemothorax was

**Albamycin (novobiocin sodium), The Upjohn Company.*

**Table 1.**—*Data in thirteen cases of resection of aneurysms of the descending thoracic aorta—Cleveland Clinic Hospital*

| Case number | Age, years | Sex | Symptoms | Cause | Date of operation, month/year | Type of graft |
|---|---|---|---|---|---|---|
| 1 | 59 | M | Pain | Arteriosclerosis | 7/57 | Homograft |
| 2 | 33 | M | None | Trauma | 8/57 | Homograft |
| 3 | 56 | F | None | Arteriosclerosis | 6/58 | Homograft |
| 4 | 49 | M | None | Arteriosclerosis | 6/58 | Homograft |
| 5 | 53 | M | None | Arteriosclerosis | 10/58 | Homograft |
| 6 | 58 | M | Acute back pain | Dissecting arteriosclerosis | 10/58 | Dacron |
| 7 | 50 | M | Pain | Arteriosclerosis (positive serologic test) | 3/59 | Dacron |
| 8 | 57 | M | Severe pain | Arteriosclerosis (positive serologic test) | 4/59 | Dacron |
| 9 | 49 | M | Pain | Syphilis | 2/60 | Homograft |
| 10 | 68 | F | Pain | Dissecting arteriosclerosis | 5/60 | Dacron |
| 11 | 52 | M | Respiratory obstruction | Arteriosclerosis | 9/60 | Dacron |
| 12 | 69 | M | Pain | Arteriosclerosis | 2/61 | Dacron |
| 13 | 47 | F | None | Trauma | 3/61 | None, end-to-end anastomosis |

seen, indicative of a late anastomotic leak. This was the first patient in the series and, although probably now he should undergo reoperation, his only treatment was several needle aspirations. It was gratifying to see the hemothorax progressively shrink and eventually disappear. Another patient had to be returned to the operating room 18 hours after the completion of his operation because of persistent bleeding. The bleeding was from veins in the posterior mediastinum related to the hemi-azygos system.

The third major complication was a hemorrhagic diathesis first noticed coincident with the completion of the operative procedure. This man bled not only from the wound but also from the upper gastrointestinal tract and the tracheobronchial tree. Early postoperative roentgenograms showed evidence of diffuse bilateral parenchymal pulmonary hemorrhage. Laboratory study revealed no hemolysis; his clotting time was normal; fibrinogen was normal. The prothrombin time was moderately prolonged. He was given eight direct fresh-blood transfusions immediately after surgery, which solved the bleeding problem; however, it was necessary to support his respiration artificially via a cuffed tracheotomy tube for five days while pulmonary changes resolved.

**Table 1.**—*Concluded*

| Case number | Complications | Result | Follow-up |
|---|---|---|---|
| 1 | Late leak | Good | Died 3 yr. postoperatively |
| 2 | Postoperative bleeding | Postoperative death | — |
| 3 | None | Good | Living and well |
| 4 | None | Good | Living and well |
| 5 | Enteritis staphylococcus (?) | Died 1 wk. postoperatively | — |
| 6 | Reoperation for bleeding | Good | Died 2 m. postoperatively, gastrointestinal bleeding |
| 7 | None | Good | Living and well |
| 8 | None | Good | Living and well |
| 9 | Hemorrhagic diathesis | Good | Living and well |
| 10 | Postoperative dissection, chemothorax | Postoperative death | — |
| 11 | None | Good | Living and well |
| 12 | Late empyema | | Died 2 m. postoperatively |
| 13 | None | Good | Living and well |

## Comments on Technic

The major hazard in aneurysm surgery is that of hemorrhage, which will usually be from the aneurysm itself. To minimize this hazard we believe that it is important before actual dissection of the aneurysm to attempt to mobilize and to encircle with tapes the aorta proximally and distally to the pathologic area. As has been discussed, the shunt's having already been prepared, one is ready to occlude the aneurysm from the circulation and to utilize the shunt at a moment's notice. With the situation under control in this fashion, dissection of the aneurysm proper can be carried out with relative safety, and frequently the entire aneurysm can be mobilized before occluding the aorta. When the aneurysm proves to be adherent to the hilum of the lung, or it invades the vertebral bodies, the surgeon should early abandon circumferential dissection, should occlude the aorta, should divide the aneurysm at one or both ends, and should excise it from above downward leaving in situ any segment of wall the removal of which seems unusually hazardous.

This approach may greatly reduce operating time and, with the bulk of the aneurysm removed, more delicate dissection of critical areas can be readily carried out.

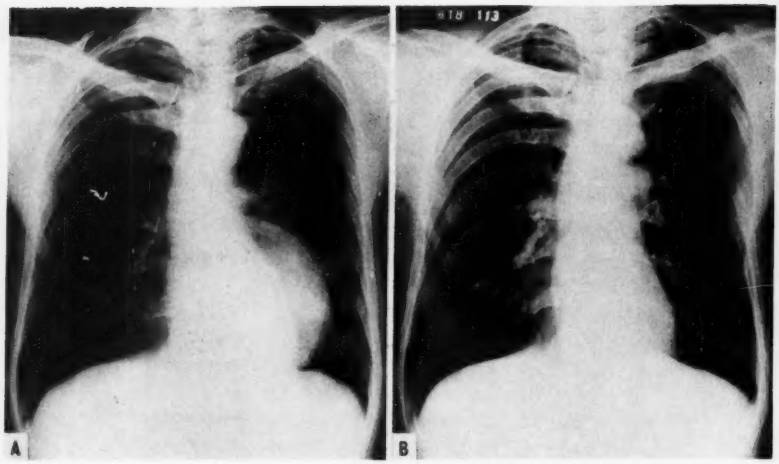


Fig. 4. A, Preoperative, and B, postoperative roentgenograms of the only definitely syphilitic aneurysm in the reported series of patients. Syphilitic aneurysms do occur distally to the aortic arch. Radicular back pain was this patient's only significant symptom.

An area where extremely troublesome bleeding can occur lies between the aorta and the vertebral bodies. This area is traversed by the hemi-azygos venous system, which is highly variable and seems to dilate in these cases, as if obstructed by the aneurysmal mass. Bleeding from this area necessitated reoperation in one patient and may have been the cause of one postoperative death. Ideally the surgeon should keep his plane of dissection close enough to the aneurysm to avoid these veins, but unfortunately what amounts to a venous lake may be inadvertently entered. Pressure in these channels is low, and bleeding can be readily controlled by packing; but before completion of surgery, all tributaries to such a lake must be carefully suture ligated.

This operative experience covers the time interval during which there has been transition from freeze-dried homografts to the use of woven crimped Dacron prostheses at the Cleveland Clinic. In six patients a homograft was used and in six patients Dacron was used. To date, both have been equally satisfactory. There have been no early or late graft failures.

One case of traumatic aneurysm was treated by direct end-to-end anastomosis without graft. On opening this aneurysm the two ends of the aorta were readily apparent, separated by more than 2 inches, and connected by a fusiform false aneurysm. After trimming away the false sac, there was sufficient residual elasticity to the aorta (one year after an auto accident) to permit direct suture approximation *(Fig. 6).*

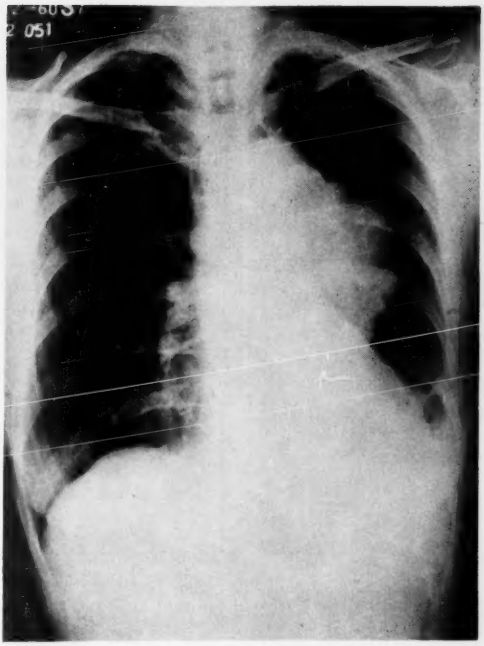

Fig. 5. Roentgenogram of what proved to be a localized dissecting aneurysm in a 68-year-old woman. Operative removal and graft were uneventful, but in the immediately postoperative period in this patient a fresh full-thickness dissection developed immediately above the upper anastomotic line, and she died.

## Discussion

The ultimate fate of any untreated aneurysm in the chest, as elsewhere, is steady enlargement and eventual rupture. This sequence may require a varying time and may be delayed by laminar mural thrombus. The life history of an aneurysm may be complicated by pain from bone erosion, mechanical interference with adjacent viscera, and rarely peripheral emboli from intraaneurysmal thrombus.

Evidence of an aneurysm may be an incidental finding in a roentgenogram of the chest. Such an asymptomatic aneurysm is apt to be the simplest to deal with technically, as the lack of symptoms suggests absence of encroachment on adjacent structures. Once an aneurysm becomes symptomatic, the symptoms tend to become progressive and intractable, and the surgical indications become urgent *(Fig. 7)*.

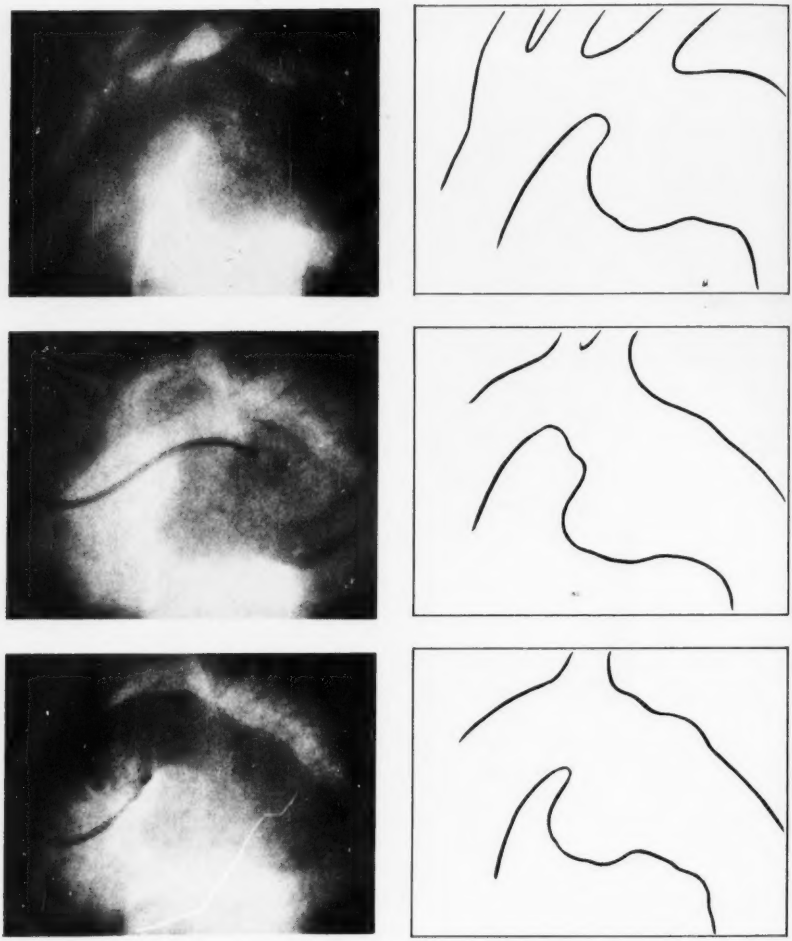

**Fig. 6.** The three photographs on the left represent enlargements of individual frames of 35-mm. motion picture films of selective cineangiographic studies in a 47-year-old woman, one year after an automobile accident. The line drawings on the right are tracings from the same frames to orient the findings. This is the typical location for traumatic aneurysm of the thoracic aorta. When this aneurysm was opened it was found to be a false aneurysm containing the two ends of aorta separated by just more than 2 inches. The false aneurysm was trimmed away and a direct end-to-end anastomosis was made.

The initial formation of an aneurysm requires the presence of a weak area in the aortic wall, which bulges or fractures under the pressure of the contained

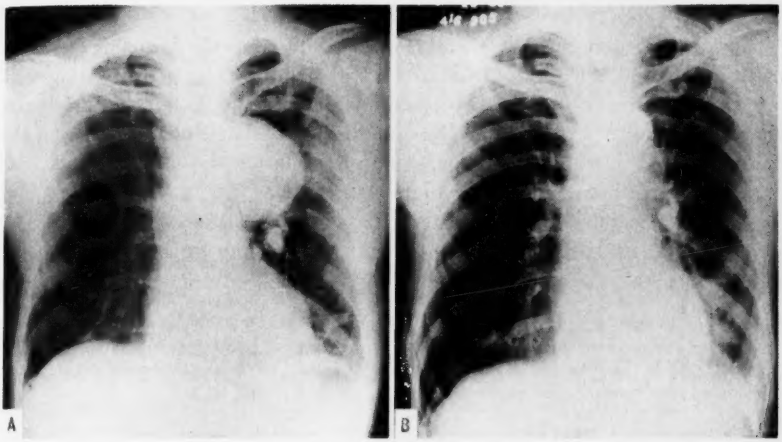


**Fig. 7.** A, Preoperative, and B, postoperative roentgenograms in a 57-year-old professional golfer. The patient's hospitalization was precipitated by severe, progressive, chest pain, and this aneurysm is known from serial roentogenograms to have enlarged rapidly. At operation there were several areas of extreme thinness, and rupture was imminent.

blood. The pathogenesis of this weak area may be due to diseases such as arteriosclerosis or syphilis, or to trauma; however, once the enlarging has commenced, physical principles readily explain why steady progression will then occur. Bernoulli's principle states that in a flowing hydraulic system the pressure is inversely proportional to the speed of flow. An aneurysmal segment of vessel has an increased cross-sectional area; therefore, flow velocity is lowered, and the pressure is higher than in the vessel of normal caliber at either side. LaPlace's law states that with equal pressure the tension in the wall of a vessel is proportional to its radius; hence, if the aneurysm has double the radius of the host aorta, the tension in its wall will be double that in the aorta per se. Thus, when a weak area commences to dilate, hydraulic principles place a steadily increasing stress on the wall, and a vicious cycle is initiated.

The facts discussed above give strong objective arguments for resection of aneurysms. The surgeon knows, however, that in most instances he is operating on an elderly patient with degenerative vascular disease. He is entitled to use his discretion in accepting patients for this type of surgery, as patients will be seen in whom there is extremely small "salvage value." However, one is obliged to offer surgery to most of these patients, and, in view of the demonstrated success in the present relatively small series, we expect to be increasingly confident in advising operation for such patients in the future.

## Summary and Conclusions

Surgical experience with 13 patients with aneurysms of the descending thoracic aorta is reviewed. Of these 13, seven are still living. Three patients died postoperatively in the hospital, and three deaths occurred late, as long as three years after operation. A bypass from the left atrium to the femoral artery for the maintenance of distal aortic circulation during occlusion was used in all of these patients, and has been proved to be highly satisfactory.

Inasmuch as most of the patients were elderly, and underwent operation for degenerative (atherosclerotic) disease, the over-all results are gratifying.

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# EVALUATION OF THE INFERTILE COUPLE

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FERTILIZATION is an exceedingly complex process involving many fundamental questions of cellular biology. Each year our knowledge increases and with this our understanding of the biochemical aspect of reproduction. The entire mechanism is related to emotional as well as physical health. Hormonal production is dependent upon stimuli from the cerebral cortex, the hypothalamus, the pituitary, the adrenals, the thyroid, and the ovaries. Only recently has the amazing interrelationship of these hormones been appreciated.

Study of the infertile couple must show whether or not male and female gametes are produced and whether or not the passageways needed for their union are patent. It must also show whether or not physiologic and biochemical functions of the female reproductive tract are favorable to migration of spermatozoa, to transfer of the ovum to the fallopian tube, to fertilization of the ovum, and to growth of the resulting embryo.

For fertility, there must be an orderly sequence of biochemical changes and coordinated muscular activity in the female reproductive tract. Such an environment is dependent on general health, normal functioning of many endocrine glands, and the ability of the reproductive system to respond to changing biochemical stimuli. Stress, caused by illness, fear, or frustration, has a significant effect on the ability of the reproductive tract to function normally.

The purpose of this paper is to discuss the procedure we use at the Cleveland Clinic to study the infertile couple, to show how the results are used to evaluate the causes of infertility, and to point out the factors that are most important in evaluating the probability of pregnancy. The procedure is planned so that absolute cause for sterility if present may be found early, in the interest of saving the couple time and unnecessary expense.

## Initial Interview

Both husband and wife are urged to be present at the initial interview. This gives the physician an opportunity to determine whether or not severe emotional problems exist in this marriage which would make pregnancy undesirable. Presence of both husband and wife also provides opportunity to expose fears the couple may have, to alleviate them if possible, and to lay the groundwork for the couple's cooperation. The understanding that can be developed in the interview helps to assure completion of the necessary tests, and often is effective therapy. The couple is given a sheet of typed instructions describing tests that require special preparation or that must be performed at specific times in relation to the day of ovulation.

During the initial interview, medical histories of the husband and the wife are recorded, and a physical examination of the wife is performed. When pelvic surgery has been done, a record of pelvic findings, and a pathologist's report is obtained from the hospital where such surgery was performed. The wife is questioned in detail about menstrual, sexual, and marital histories. Menstrual history includes age at onset of menstruation, amount of flow, occurrence of dysmenorrhea, and thorough discussion of any change in regularity. Sexual history includes data on frequency of coitus, whether or not lubricants are used, frequency of orgasm in the wife, and whether or not dyspareunia is a problem. Information as to whether or not pregnancy was ever achieved in the wife, or by the husband, in this marriage or in previous marriages is valuable.

During a complete physical examination, endocrine stigmata are noted. Distribution of fat and of hair, texture of skin, span-to-height relationship, and shape of the hands are significant. Hereditary and physical defects that would make pregnancy inadvisable or impossible are evaluated.

The first step in the pelvic examination is inspection of the cervix by means of the speculum. Papanicolaou spread of cervical secretions is taken for cytologic study. Cells of the vagina are obtained on a swab, and are then suspended in saline solution to determine the presence or absence of vaginitis or cervicitis. When *Trichomonas* or *Monilia* are found, treatment is initiated at once. Suspicious lesions of the cervix are biopsied. A small, elongated cervix is indicative of inadequate ovarian function. The position of the cervix is of little importance in the process of insemination unless the uterus is fixed in a retroverted position. The pelvis is systematically examined for ovarian pathologic change, endometriosis, and uterine abnormalities.

At the first interview we routinely order a Wassermann blood test, a complete blood count, urinalysis, and blood sugar determinations. When no absolute cause for sterility is found, blood typing, and determination of basal metabolic rate and of serum protein-bound iodine concentration are also included.

## Diagnostic Infertility Studies of the Husband

The procedure for collecting semen is given to the husband at the first interview, with the request that the specimen by obtained after abstaining from coitus for four days. The specimen is obtained by friction unless this is contraindicated by religious considerations. In such cases the husband may have intercourse and may use a special perforated plastic sheath that does not affect the motility of spermatozoa. The specimen is brought to the laboratory within an hour after collection. Volume, viscosity, pH, the number of spermatozoa per milliliter, and the total number are determined. Motility is graded on a scale of 0 to 4+ then, and again after four hours. Any unusual characteristics of the specimen, such as agglutination of the spermatozoa, are noted. A stained slide is used to study the

morphologic characteristics of the spermatozoa. We use the MacLeod standard for normal semen; namely, a minimum of 20 million spermatozoa per milliliter with 40 per cent showing good linear progression and 60 per cent having normal form; the most important single factor is the quality of motility, that is, the percentage of the spermatozoa that show good linear progression.[1]

When the semen fails to meet this standard, the analysis is repeated, and the husband is referred for complete physical examination to the endocrinologic service. Standard laboratory studies, as listed for the wife, are performed; endocrine assays are made when necessary. These often include determination of the basal metabolic rate, the serum protein-bound iodine, and less often the urinary 17-ketosteroids and pituitary gonadotropin. When azospermia or severe oligospermia is present, the husband is referred to a urologist for testicular biopsy and other urologic tests.

## Diagnostic Infertility Studies of the Wife

In the event that spermatozoa show good linear progression, we proceed with special fertility tests of the wife to evaluate the uterus, the fallopian tubes, and the cervix. Only if the husband has been known to produce pregnancy do we proceed with these tests without obtaining a semen analysis.

*Tests of fallopian tubes.* To eliminate the fallopian tubes as the cause of the infertility, it is necessary to establish that the tubes are open and that their functioning is normal. Three structures are important: (1) the musculature, (2) the cilia, and (3) the endothelium. The Rubin test and the salpingogram will show whether or not the tubes are patent. The kymographic record taken during the Rubin test shows the amount and the variation of pressure in the fallopian tubes. This gives some indication of muscular physiologic activity, since Hartman and Stavorski[2] demonstrated that the fluctuations in pressure are caused by the activity of the fallopian tubes alone.

All secretions of the female reproductive tract vary with the concentration of estrogen and progesterone. These will be discussed under the evaluation of ovarian function. It is known that the cilia of the fallopian tubes move 20 per cent more effectively at the height of estrogen production at ovulation[3] than they do postmenstrually. No tests have yet been devised which can be used routinely to demonstrate the efficiency of the cilia in transfer of the ovum in the fallopian tubes.

Precautions are essential when the Rubin and salpingogram diagnostic tests are made, because these procedures require invasion of the abdomen. There must be no infection present in the pelvis. Carbon dioxide gas is used in the Rubin test, and a suitable physiologic solution for salpingography. Both tests must be performed before ovulation. It is helpful to do the Rubin test only a few days in advance of ovulation, so that the kymograph will indicate the conditions present

when fertilization would be occurring. The pressure within the uterus must be known at all times and must not exceed 200 mm. of Hg.

The sources of error in doing these tests can be minimized by checking the apparatus for patency and leakage, by good technic in performing the test, and by allaying the patient's fears; fear may cause spasm of the fallopian tubes. Before the test is started, the position of the uterus is determined so that the cannula can follow the direction of the cervical canal without pressure, unless stenosis is present. To minimize pain, no tenaculum is used for the first test. The carbon dioxide is allowed to flow at the rate of from 20 to 30 ml. per minute, thus gradually increasing the intrauterine pressure. If leakage occurs the tenaculum can then be used. The fallopian tubes are considered to have normal patency if rhythmic oscillations occur which are characteristic of normal tubal function. These are in the range of 60 to 120 mm. of Hg, with oscillations that vary from 10 to 20 mm. of Hg. Such a finding must be followed by shoulder pain, when the patient sits up, for the diagnosis of a patency to be absolute.

Failure of carbon dioxide gas to pass through the fallopian tubes does not prove permanent obstruction, because spasm, thick mucus, or torsion of the tubes caused by adhesions may exist. When obstruction is encountered, we believe that the Rubin test should be repeated at least three times, preceded by the administration of antispasmodics, before a diagnosis of permanent obstruction is made. When a pressure of 200 mm. of Hg is maintained for several minutes it will often be followed by a flow of gas at normal pressure levels of from 80 to 100 mm. of Hg. All subsequent tests may continue to show a flow at this pressure. The Rubin test may therefore be therapeutic as well as diagnostic.

The salpingogram gives information concerning both the uterus and the fallopian tubes, and is a means for identifying congenital abnormalities, tumors of the uterus, and the location of tubal obstruction. This information is essential before a decision is reached concerning possible surgical therapy. The effectiveness of tubal surgery varies greatly with the location of the obstruction and the skill of the surgeon. Morton[4] states that salpingolysis results in about a 30 per cent pregnancy rate. Implantation of the uterine end of the tube into the uterine cavity yields about 10 per cent success.

*Ovarian function.* We use three procedures to evaluate ovarian function: (1) the basal body temperature, (2) endometrial biopsy studies, and (3) examination of the cervical mucus. Basal body temperatures are of great help, but they are frequently misused. They give information as to whether or not ovulation occurs, the approximate time it occurs, and some indication of the amount of progesterone produced after ovulation. When ovarian function is poor, even though ovulation occurs, the elevation of temperature may be so slight that ovulation can only be confirmed by endometrial biopsy studies. In most cases the temperature changes are sufficiently pronounced to be useful to time the Rubin, postcoital, and

endometrial biopsy tests.

The temperature chart may be used by the patient to time coitus with ovulation. This should be done only after she has received instruction from the physician concerning the advisability of such a procedure and its timing; tensions produced by the necessary procedural exactness may be detrimental to fertility. Because a basal body temperature rise takes place after ovulation, and because an unfertilized ovum will live only from 6 to 12 hours,[5] coitus after temperature rise will not result in pregnancy.

The endometrial biopsy study gives proof as to whether or not ovulation has occurred. The pathologist can see the changes in the endometrium produced by progesterone, and can evaluate whether or not they are comparable with the changes expected in the highly fertile woman.

Cervical mucus will change in physical and chemical properties with changing concentrations of ovarian hormones. In the absence of infection, repeated tests of mucus give accurate information concerning the day of ovulation. Postcoital tests demonstrate whether or not the mucus is favorable to the migration of spermatozoa. To make this evaluation we ask the couple to have intercourse at the time of ovulation, following abstinence for three or four days; the female partner is asked to remain in bed for one hour. Six to eight hours later the wife is examined. Mucus aspirated from the cervix with a pipet is put on a slide over which a cover glass is placed. The spinnbarkeit of the cervical mucus is measured. (The number of centimeters to which the mucus can be stretched before breaking is called spinnbarkeit.) Immediately premenstrually and postmenstrually the spinnbarkeit is from 1 to 2 cm. As the estrogen concentration increases before ovulation, the breaking point of mucus increases to between 10 and 15 cm. The day of maximum spinnbarkeit in the human female is the day of optimal receptivity to sperm. Maximum spinnbarkeit is found to occur just before the postovulation temperature change.

The mucus is allowed to dry on the slide after the spinnbarkeit test. It is then examined under the microscope to determine whether or not crystallization with arborization, called "ferning," has resulted. Roland[6] showed that ferning was related to high concentrations of estrogen, and that it occurred particularly at the time of ovulation. Campos da Paz[7] pointed out that progesterone inhibits fern formation.

Mucus from the mid cervix is placed on two slides, one to be stained with the Papanicolaou stain for later evaluation, the other for immediate study of sperm motility, the presence or absence of leukocytes, and an estimation of the percentage of cornified cells. Under a cover glass, this slide is examined under the microscope with a high-power, dry objective with a 10X ocular. The number of spermatozoa per high-power field is counted in at least four areas. The percentage of the spermatozoa that show good linear progression is determined,

as well as the percentage which are motile but show no progression, and those that are nonmotile.

Absence of migrating spermatozoa in the postcoital test requires the study of cervical, seminal, and ovarian factors. Endocervical infections may be present without evidence of a lesion on the external surface of the cervix. All cervical infections should be treated, even though there is considerable controversy about the relation of infection to fertility and, specifically, to sperm migration. Many pregnancies occur when cervicitis is present; yet Grant,[8] who reported on 5000 postcoital tests performed in his infertility clinic, stated that when spermatozoa did not migrate into the mucus, 70 per cent showed the presence of polymorphonuclear leukocytes in the cervical mucus. His over-all incidence of subfertile seminal assays was 42 per cent; this would seem to be significant.

From the second slide, stained with Papanicolaou stain, the percentage of cornified cells is determined. Other characteristics are rated on a scale from 0 to 4+; these include mucus, trichomonads, spermatozoa, white blood cells, histiocytes, and bacteria. When less than from 75 to 90 per cent of cornified cells is found on the slide, we first determine whether or not the test was done from 14 to 16 days before the onset of menstruation. If it was not, the test is repeated in the next cycle at or just before ovulation. Also, during the next cycle, serial vaginal cytologic studies may be done to determine the day of maximum cornification. When the postcoital test shows few migrating spermatozoa and there is less than 50 per cent of cornified cells at ovulation, the patient is referred for endocrine evaluation. Basal metabolic rate, serum protein-bound iodine and serum cholesterol concentrations are determined. Urinary tests of gonadotropin, 17-ketosteroid, and other factors are performed as indicated.

When there is good sperm migration, even though the percentage of cornified cells is less than 50 per cent, the patient is not referred to the endocrinologist until other factors that might be causing the infertility have been carefully reviewed and have been evaluated. It should be remembered that the finding of many motile spermatozoa and a high percentage of cornified cells does not necessarily mean fertility, because anovulatory cycles will frequently show from 80 to 90 per cent cornified cells for many days, with sperm survival for two to three days.

Treatment with hormonal therapy for improvement of cervical mucus must be given with a thorough understanding of the many metabolic interrelationships of the hormones produced by the pituitary, adrenal, ovary, and thyroid glands. It must be remembered that estrogen will stop ovulation if given in large doses; and even small doses, given three to four days before expected ovulation, may be followed by an anovulatory cycle or amenorrhea.

## Discussion

Our knowledge concerning the biologic changes occurring at the cellular level

in the process of reproduction is rapidly increasing; as tests are developed to demonstrate more of these changes, there will be fewer patients in whom no cause for infertility is found.

New tests must be developed for more accurate evaluation of the quality of motility and fertilizability of spermatozoa. New tests are needed to show how effectively the fallopian tubes serve their function in transferring the ovum and, finally, more tests are needed to show how well the uterus and the ovary function for the growth of the embryo.

Infertile couples should be completely evaluated within one year of failure to conceive. This interval should be less if the wife is more than 25 years of age. MacLeod, Gold, and McLane[1] have shown that 40 per cent of wives of infertile couples conceived within one year when the fertility of both husband and wife were rated as good; this decreased to 18 per cent when the wife was more than 25 years old. It is urgent that the couple be evaluated while the chances of success of pregnancy are the highest.

## Summary

The evaluation of the infertile couple requires a detailed study of the reproductive anatomy and physiologic processes of both husband and wife, and how well these function as a biologic unit.

Our procedure for this evaluation has been outlined. It has been shown that it is insufficient to demonstrate that there is patency of the female reproductive tract, whether or not motile spermatozoa are being produced, and whether or not ovulation is occurring. The physiologic and biochemical factors in reproduction must be evaluated for accurate diagnosis of the cause or causes of infertility.

Studies of cervical mucus are considered to be a gross method of evaluating the biochemical factors in the female reproductive tract as a favorable medium for migration of spermatozoa. New tests are needed for adequate evaluation.

The number of successful pregnancies resulting from evaluation and treatment of the infertile couple will be proportional to the age of the wife, the completeness of the evaluation of the couple when they first consult the specialist, and the cooperation of the couple in completing a scientifically planned course of treatment.

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# A WHITHER REPORT ON THE RESEARCH DIVISION OF THE CLEVELAND CLINIC: A COMMENTARY ON RESEARCH TODAY

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*Division of Research*

THIS report reflects the view of one person, currently the Director of Research of the Cleveland Clinic. I hope, however, it is not a minority point of view. It represents my cogitations after 16 years of experience in the Division. Some facets of only contemporary interest are included to provide a truer picture of the problems we face from year to year. Some small rubs and irritations must surely show through. There has been no attempt to cover them up with soothing verbiage. Rather, I have attempted to present an instant in the reality of the conduct of research.

The report is meant for those everywhere who are interested in the organization of research, for those who support research, and for those who suffer from the diseases that will be benefited by the fruits of this sort of research.

## The Changing Scene in the World of Research

I have had the interesting experience during my professional life of seeing a complete reversal of public attitude toward research. When I started in 1920, the attitude was one of complete indifference on the part of the public, and most physicians. As you are well aware, since about 1946, our era has suddenly become an "age of science." I am sure I hardly need convince you of this when most "growth" companies are now spending from 6 to 10 per cent of their wealth on research. Former President Eisenhower's Science Advisory Report reflects this change when it says, "Scientists have become one of the nation's most valuable resources." President Kennedy's health message calls for a "vast expansion of medical research." And lastly the Report of the President's Conference on Heart Disease and Cancer makes the firm recommendation for "a much higher level of federal appropriations in support of medical research in the fields of heart disease and cancer and a commensurate increase in voluntary contributions."

And what are the nation and the present administration going to do about it? Again, I quote, "American science in the next generation must, quite literally, double and redouble in size and strength. This means more scientists, better trained, with finer facilities." There can, in my opinion, be no doubt that this doubling has already started. As one report puts it, "The training of scientists takes longer than it used to and the facilities needed are much more complex and expensive." It is only a question of a short time when competent research workers are going to be at a great premium. It is possible that many places will find themselves with fine facilities but nobody of excellence to use them, which is the reverse of the situation just a few years ago.

Our problem in our own laboratories is to create, and to maintain, an atmosphere in which creative research can be most effectively done. Deflection from this purpose, no matter how seemingly cogent the argument, can only result in less important and less original output; it is the net output of creative work of excellence that determines the worth of a research division.

## Investment in Science

Until recently, support of research was considered charity. A sharp change has occurred and it is now a prime investment. In fact, there have been almost no speculations, let alone investments, which have paid off so handsomely both in money and improvement in the material aspects of the social scene. "We are only just at the beginning of the use of scientific investment in the large sense and the returns it can bring in are literally incalculable." It seems to me that we are at the beginning of the scientific revolution, just as a century and a half ago we began the industrial revolution. From the actions of Congress, the Bureau of the Budget, and the President's directives, it is now clear that research support will not be withdrawn according to a caprice of Congress. We, in particular, were unwilling at one time to accept any further support from government because we feared it to be "soft money."

No one today can say how rapidly this great industry of discovery will grow. The President's report says this: "Any shortsighted calculation of return on investment is likely to be self-defeating. Scientific progress does not occur in any neatly predictable way." The evidence is now clear that support from government on a large scale is occurring and will accelerate.

There are also changes in the way money is being given and how it may be used. The trend is to give maximum flexibility and stay away from the restrictive plans of a few years ago.

## Basic Versus Applied Research

Until quite recently, and to a degree even today, an argument was being carried on which purports to prove that so-called basic or "program" research stands in direct opposition to applied "practical" or "clinical" research. This has been a futile waste of time and has misled many well-meaning people. The quicker the whole question is dropped the better. One striking characteristic of our new scientific age has been the gradual disappearance of this distinction. There is no such thing as "impractical knowledge." The same individual is often both a "pure scientist" and, for example, an engineer. He may well be both an "impractical" pharmacologist and a good bedside doctor. Thus, distinctions of this sort are poor ones on which to build plans. Gains in knowledge must not be labeled and pigeon-holed as practical or impractical. Rather they should be kept before all, for use as needs arise.

## History of the Organization of the Research Division of the Cleveland Clinic

Doctor Corcoran and I came to the Cleveland Clinic early in 1945 to organize an entirely new research division. Those were war years and we had to "make do" with what we had, not with what we would have liked. Thus, many changes that should have been made were not made. We have remained in a number of respects on the original "make-do" war footing.

We had what we think a unique plan. Instead of breaking the Division up into a series of small, unrelated cells called "departments," the whole group was thrown together as a unit, working on a central theme. The group was organized around the problems, in our case hypertension, arteriosclerosis, and brain chemistry. This scheme, over short periods, is sometimes not so flattering to the ego of the individual as is strict departmentalization, but in the long run has proved more satisfying because of greater work output and sense of achievement resulting from the actions of the whole group. I am convinced that the effectiveness of some professional investigators under this system is much greater, in terms of advancing the problem, than that of several other types of organizations. This is not a plan for the "lone wolf" type of investigator.

To keep our work oriented toward the problems of medicine, beds in the hospital were set aside for our patients and we started our own outpatient group. These patients are fully cared for by us and have been the starting point of all of our major research problems. This arrangement has proved of inestimable value. In this way the Division has achieved a certain homogeneity in which the disciplines that represent it all contribute to the same general operation. Patient care and structural organic chemistry rub elbows, as do physiological and physical chemical research. I believe this a unique and valuable contribution to the organizational scheme of medical research and, in the future, the principle should not be lost. Pulling away of the individual from this structure is easy to do for the sake of immediate expediency, and if this is carelessly acceded to, the whole structure shortly disintegrates. I feel strongly that if this unifying principle of organization around the solution of major problems is lost, the research effort in our case will be greatly reduced in effectiveness. I can assure you from long experience that disintegrative forces are constantly at work to break the group effort into small independent units.

## The Nature of the Problem

Small organizations are always faced with the problem of how much of a major problem they should undertake to solve. Because of the fact that the understanding of cardiovascular diseases had not advanced signally until the past decade, we felt impelled to take a broad approach, hoping that the problems would narrow and would deepen with the passing of time. For example, diet soon became a

major aspect of the problem of heart attacks. To study diet in its relationship to patients, a research kitchen had to be set up. Because of the success of this work, the Government asked us to plan, and to set up, a major dietary study aimed at broad testing of the proposition that practical change in the American diet might lead to lessening of the numbers of heart attacks. You will now see why there is no dividing line between basic and applied research.

Let us take another problem, this time concerned with hypertension. We had for many years been studying the problem of the control of the caliber, or diameter, of blood vessels by the nervous system, for if the caliber is reduced, blood pressure goes up, as during a fit of rage, and goes down when the caliber increases. We were constantly on the lookout for chemicals that would block this action of the nervous system. Many hundreds were tested in association with drug manufacturers with greater, or lesser, success. At present, one drug, called "guanethidine," has proved in our patients as well as in our dogs with hypertension, to be highly effective. As more knowledge is gained through research, still more useful drugs will become available. We now feel confident that with proper care, most high blood pressure can be controlled and the patients' lives greatly lengthened.

I want to impress on you the variety of skills that is required to solve problems as varied as these. It is for this reason that we have enlisted the aid of organic and physical chemists, biophysicists, pharmacologists, pathologists, physiologists and statisticians—all concerned with the same problems. There is need for still more of these disciplines to be added, which is what I have called "the conduct of research in depth."

We have tried, inasmuch as is possible, to take problems from our patients and transfer them to the laboratory for solution. It is for this reason that our clinical work has been such an important aspect of our research. But when the problems reach the laboratory, we must demand that the research be worthy of the subject. By this, I mean research of depth and penetration. Until recently, in the field generally, there has been much superficial work that will not withstand deeply probing criticism.

## The Problem of Maintaining a Research Staff

We face a serious disadvantage in research in clinic practice, when compared with universities, in that we do not have the continuous stream of stimulating young minds to work with us. Most of our staff is recruited from young people who have recently acquired their degrees. Sometimes we choose well and the man becomes a permanent part of our staff. Often we must let them go because we do not believe they will grow into the caliber of men we want on the staff. Thus, we look at all new people as candidates for staff, in marked contradistinction to universities, which, because of numbers, must let many go elsewhere.

Twenty years ago the research market was glutted with brains. Today it is

just the reverse. I suggest that during the next 10 to 20 years, the major problem in research is going to be to find, and to hold, high-grade talent. In the past few years we have lost some valuable people. However, this does not mean that we have come to the end of opportunity in medical research. The quality of the young men and women to pick from has not seriously deteriorated, despite the fact that other research laboratories and, in particular, the universities now have the money with which to compete.

My strongest plea is to insure that young people constantly pass through the Research Division so that a few can be selected and kept. If this is not done, the quality and quantity of the staff could deteriorate dangerously. It is all too easy to pass from excellence to mediocrity without even realizing it.

## How Big

I have said for the past 16 years that there is a limit to the size of our Research Division. I have never believed that the most creative research came from enormous, impersonal institutions, universities or otherwise. There are certain simple criteria that I look for: the organization should be small enough so that:

1) Everyone can know everyone and see most nearly every day.
2) Few formal meetings are necessary.
3) Mutual exchange of information can occur expeditiously and informally.
4) Equipment may be used by everyone with minimal effort and rules.
5) The spirit of unity is everywhere to be found.
6) Elaborate and impersonal rules and regulations do not have to govern the group.

In my opinion, the physical boundaries of the Division are about right. Improvement here and there is very desirable, and in some cases essential, but these are not big things. Flexibility is essential. Research, as you well know, does not lend itself well to rigid planning. When you find you can plan too easily, the signal flags of danger are up; you are no longer doing creative research. If you are going to get in a rut and follow it, choose the rut well because you will probably be in it for a long time.

No one can say what a research division will be like in 10 years. I would hope no one would want to say. I am certain if there are sensible, competent people running it, the Division will add importantly to knowledge of its chosen fields. If you try to substitute rigid plans or committees for able people, I will predict the Research Division will cost the same, or more, but its productivity will have deteriorated seriously. A negative and constantly restrictive atmosphere created by a nebulous fear that somehow research will overgrow other activities of a great clinic is groundless, and if credence is given this fear, it can ultimately erode the creativity of groups such as ours. This is an aspect of research that is

hard to sense and to recognize. Perhaps it is best characterized by the "spirit of the place." Lose it and you will soon find how important it was.

Except in its broadest sense, I cannot tell how big a research division should be. I can tell you how good it should be. I would prefer to leave to my successor the planning of his future because I cannot tell whether he will be concerned with "outer space medicine" or the more earth-bound problems which have so excited us. I would prefer to count on the common sense and wisdom of personal leadership than attempt an impersonal blueprint for the future.

I would want no curb on the intellectual bigness of a research group but physical bigness has definable upper limits which should be determined by common sense in the maintaining of excellence.

## Consolidation of the Research Division

I believe that all organizations that are effective must have flexibility. I have already said that I do not believe a research group should grow beyond certain definite limits. We must not, however, confuse growth with change. Drop-out of effective personnel is inevitable, and younger people must always be in training so that replacements may be made. Equipment must be kept up to date. There must always be some room for modest expansion for the workers who prove themselves most effective. Without this the good ones will certainly be lost.

## Communication with the Scientific and Lay World

One of the chief functions of science is to communicate with other scientists the world over. To do this requires the most painstaking care in the preparation of reports on the work that has been accomplished. In our profession, a man's reputation among his peers is one of his most cherished possessions. Not to understand this is to miss much of what goes on in the world of science.

"Personal glory" is a much misunderstood and abused phrase. I can only give you a word of advice; among good scientists, avoid the phrase, as you are almost sure to misuse it and to create misunderstanding. The creation of an "atmosphere of respect" is a difficult and often subtle thing, much less easy to measure than so many dollars' worth of a product or service. Laymen often tend to sneer at what seems to them a personal and selfish characteristic of scientists. If, on the other hand, you will think it through, I suspect you will reach a deeper understanding of the nature of science and scientists.

Perhaps I can best illustrate the nature of the problem that all good investigators face by our own experience in the synthesis of angiotensin. About 20 years ago we discovered this important substance along with Braun-Menéndez in Argentina. In the ensuing years, work has continued steadily but very slowly in our laboratory. At times only one man was concerned in the isolation of a substance that may well be the cause of a major type of high blood pressure. Our

total group of investigators was that small. Such a situation would be inconceivable in the field of, say, cancer research. About eight years ago a well-equipped and intelligent team of workers at the Crile Veterans Hospital also started on the quest. We were for a long time unaware of the competition. Concurrently a team in London, England, began as well. The result was that within a short period the structure of this complex substance had been determined by these groups. The only way we could save our position in the field was to synthesize angiotensin. With only two people to carry this out, we were amazingly fortunate to be able to accomplish it at the same time a group of nine chemists at the Ciba Company in Basel, Switzerland, announced its synthesis. Had we not been lucky and the two men not highly skillful, we could well have lost out entirely in the field which we opened. While the outsider may say what difference does it make who discovers something, remember the research worker has only one salable product and that is his reputation.

The desire to communicate, of course, in part springs from the fact that until people accept a piece of work it is not included in the body of verifiable knowledge. To do it well is to create an atmosphere of respect. Writing and lecturing are two of the few legitimate ways of exhibiting the excellence of research to doctors and laymen. There is often a tendency to disparage this type of public relations because tangible results are often hard to measure. One of the simplest measures is the kind of young men and women who want to join the staff of the Cleveland Clinic. Good ones are attracted by the contributions and persons of excellence on the staff. Good doctors want to belong to a distinguished group.

There is still another aspect of communication which concerns the participation of the research staff in the large scientific societies, government commissions or councils, or organizational activities such as the "American Diet Study." I believe these activities are of great importance but should be so regulated that they never become more than a side line. When, in general, they cannot be done in the "evenings or week-ends," except under unusual circumstances, they should be cut back.

## Project Research

I have described the program of research carried out by the Division itself. There is need for another device to implement the research needs of physicians in the Clinic. This is done by a committee composed of members from both the Clinic and the Research Division.

The proposed project is submitted to the committee in writing. After careful and sympathetic study, it is either accepted or returned for revision. An adequate budget is available to finance these projects.

Since this system was inaugurated some five years ago, there has been marked improvement in the quality of the projects submitted. Relatively few are

now denied, and most of them are completed. Years ago the mortality among research projects was shockingly high, chiefly because the would-be investigator had more momentary enthusiasm than scientific training. Our clinical staff has now learned that research has much drudgery connected with it and that to do it successfully it must for the most part be done with the physicians' own hands and brains. Research *in absentia* is seldom a success.

## Financial Support of Research

I shall observe simply that over a period of 15 years the Research Division out-of-pocket expense to the Clinic has been unusually steady. We hope that research endowment will grow. A few gifts have, from time to time, been received quite unsolicited. This has been a deeply heartening experience. The rest of the money has come from government, and at first, there was great apprehension about it. To repeat, at one time, we actually turned our backs on it. I think we all realize now, that this is "hard" money. Despite this, I hope that private donations will continue to be an important and even a vital part of our budget. The loss of private giving would, in my view, be a disaster.

I want to make my position on a budget crystal clear. I agree that a budget should be employed. I do not agree that a "top level of spending" for the next 5 or 10 years can, at present, be set.

I hope that the Research Division will keep one goal in mind — to run the Division as effectively as possible within the limits of its physical size and the mental capacity of its staff. Money is only one of the aids to the furtherance of these goals, and to set it as *the* limiting factor is irrational.

I want also to call attention to another form of fiscal problem. From time to time we have been asked by government to administer, or to participate in, some cooperative major research problem in the national interest. Recently, for example, we were requested to set up a national diet experiment. A specified sum was given us to pay committee meeting expenses and the expenses of an executive director. Little of our time is needed for this activity but a certain amount of bookkeeping is required which is adequately paid for by overhead allowance. Under no conditions, however, do I think this sort of monies should be considered as part of the research budget. To do this would destroy the whole philosophy of the spending of money on research.

The point I am trying to emphasize is that without the use of good judgment and common sense, a budget can be made to have a leaden effect, and become an almost constant source of irritation. I believe that judgment concerning expenditures must be based on long scientific experience, and that within the limits of the money available for research, the Director and the Advisory Committee must make major decisions in collaboration with the Administrative Office.

## The Purposes and Goals of a Research Division

1. Medical and surgical care is as good as the research which supports the body of knowledge on which it lives. The "better care of the patient" is therefore one of the primary purposes of a research division.

2. Research itself is worth doing for its own sake, if for no other reason than that it enriches the human spirit.

3. Research provides a constant stimulus to better and more penetrating medical practice. Its educational value is great.

I would also call your attention to the President's Commission on National Goals, the so-called "Wristen Report." Not a single working scientist was on this Commission, yet they observe that:

1. "We should allot a greater proportion of our total effort to basic research —. We should recognize that our creative activities in science and all other fields will be more productive and meaningful if undertaken, not merely to be ahead of some other nation, but to be worthy of ourselves."

2. "Available scientists must be used more efficiently. The practice of wasting highly trained people in jobs below their capacity, particularly in some defined related industries, must be eliminated."

3. The Commission feels that the next decade will see new scientific breakthroughs which may change our lives, our industries, our jobs and perhaps our whole thinking.

4. "In an age when few political decisions can be made wisely without some scientific grounding, no college graduate should be totally ignorant of science."

This report, like several others, gives a clue as to how some people of insight and integrity are thinking.

## Recommendations

1. Help to create an atmosphere in which research of the greatest excellence can be conducted.

2. Insure that there is a constant supply of young people from whom staff will ultimately be recruited. A plan for postdoctorate training would be most desirable and probably will be essential.

3. The unity and constancy of purpose of a research division should be carefully guarded. There is always danger that the activities will become splintered and the advantages of working for the common goals of solving particular problems be lost.

4. Growth should be limited to small, flexible increases or decreases in staff and equipment, wherever the need seems to exist; perhaps this had best be called "consolidation."

5. The budget principle should be kept. The spending of the budget should be under the control of the Research Director with his advisory committee in

consultation with Clinic administration.

6. The activities of a research division should not be too closely integrated with the income of the parent clinic. It should be recognized that enough funds can be obtained from outside sources to insure top efficiency.

7. I strongly recommend that every effort be made to infuse an atmosphere of stability so that every few months there is not another period of re-evaluation of research and "soul-searching" by one or another groups. The work load of research is purposely set at such a high level that even small distractions are wasteful.

8. I close this report with the thought that I do not expect that all problems will be solved with one large resolve. I hope that many of the principles on which an excellent Research Division should operate can ultimately be agreed upon and be codified, but certainly not all. Further, I hope we never get away from the philosophy in which I so firmly believe: that you cannot substitute rules for individual human decisions, and that committees cannot run an organization. To me, a research division will be only as good as the individuals who do the research and who participate in its management.

# FATIGUE AND LEISURE

A. DIXON WEATHERHEAD, M.D.
*Department of Neuropsychiatry*

IT has been said that this is the Age of Anxiety. As we advance in knowledge, as we develop culturally, and as our civilization evolves, we are beset by new fears and new dangers. Almost every day brings with it something new for us to worry about. We hear of wars and rumors of wars, and of missiles and sputniks hurtling around high overhead. We listen to talk of atom bombs and hydrogen bombs that can destroy us altogether. We have perhaps, too much power, and too little judgment to enable us to control that power. As a result of our fears, we seek various panaceas to make living less frightening and more satisfying. In the United States one in ten of us receives psychiatric help at some time during his life, and an even greater proportion of us take tranquilizers or sedatives from time to time to find peace.

Our search for peace of mind is so great that books on this subject become best sellers. Many of us use alcohol moderately as a socially acceptable tranquilizer, but millions of Americans are alcoholics. Each year for 20,000 of us the struggle for balanced living becomes unendurable, and suicide becomes the final effort; many more than this number attempt to commit suicide. It has been said that we all are neurotic—with the possible exception, of course, of a few psychiatrists—and indeed, if one is not neurotic, then one is dull—out of fashion. "Normality," someone has said, "is a species of dullness." In any event, we all, neurotic or normal, react to physical and mental stress with fatigue, and when anxiety or fear is involved, these emotions seem to act as catalysts and to intensify the fatigue.

## Fatigue

Fatigue, in response to stress, is not a phenomenon restricted to this Age of Anxiety. Fossils of human bones, taken from the Nile Valley, some of which are about 350,000 years old, show among other things that diseases such as osteoarthritis and arteriosclerosis had been relatively common diseases.[1] This evidence suggests that we may not be entirely right in attributing such disease processes to the strain and stress of present-day living. Indeed, many of the stresses of everyday living are much the same today as they have always been. One of the oldest writings in the world when translated, states: "Alas, times are not what they used to be. Children no longer obey their parents."[2]

What is fatigue? Little is written about fatigue, yet all of us are familiar with the phenomenon, for we frequently experience it. Some say it is *all* in our minds;

*From a paper presented at the City Club Forum, Cleveland, Ohio, on February 27, 1960.*

and they are almost right, for *most* of it is.

*Physical fatigue.* Physical fatigue may result from excessive physical exertion, especially when we are not used to exerting ourselves physically. Activities such as moving furniture, waxing the car, mowing the lawn, walking five miles before breakfast, digging in the vegetable garden, or carrying out the garbage, may cause us to feel physically fatigued. This is not a pathologic state; it is both healthy and desirable. No anxiety or fear is associated with it. It results in part from physiologic alterations of the muscles, and from the accumulation of lactic acid and other metabolites. Such fatigue one can readily dispel by taking a warm bath, massaging the tired muscles, and by obtaining some relaxation, rest, and sleep.

The fatigue that results from the stress of conditions such as anemia, tuberculosis, fever from any cause, diabetes mellitus, myxedema, and hepatitis, is a symptom of disease, and may be the first symptom of some diseases. When one is fearful or anxious, the fatigue experienced is much greater than when one is relaxed. This type of fatigue from the stress of disease, however, is not within the scope of this paper.

*Mental or emotional fatigue.* The type of fatigue we are particularly interested in is mental or emotional fatigue, which comes from mental or emotional stress. The stress may be acute or chronic.

*Acute emotional stress* is associated with fear. The frightening stimulus creates mental tension and apprehension, which cause the body's defenses to become mobilized for action—the so-called fight or flight reaction will occur, depending upon the nature of the stimulus. When the threatening stimulus is a mouse, the fight response may follow; when it is a circus tiger that has escaped, the most appropriate response may be flight. Whenever some kind of action is taken which is an appropriate solution to the fear stimulus, there is relief from tension. When no action is taken, or when the fear stimulus persists and inappropriate action is taken, the feelings of tension and apprehension also persist and mount, resulting in fatigue. This sequence explains why an expectant father may suffer so much more than the expectant mother at the time of her delivery. She produces a baby, and this appropriate action relieves her tension. He is limited to pacing the corridor floor, to smoking innumerable cigarettes or to biting his fingernails, which are very exhausting activities.

The inability to take appropriate action in response to fear stimuli is well known to soldiers in battle, and they may temporarily break down mentally from tension and fatigue. This is called "combat fatigue." A similar state occurs in airmen under stress; it is called "flying fatigue." Disaster victims, who are stunned by a mass of threatening stimuli, experience exhaustion or disaster fatigue. Similarly, examinees suffer from examination fatigue. When physical fatigue is concurrent with mental stress, the exhaustion is more extreme than when it is absent. A person exposed to frightening and threatening stimuli becomes tense,

anxious, and apprehensive. He is sensitive to noise; he feels weak; he trembles; he is irritable; he loses emotional control and bursts into tears easily; and he feels exhausted. The treatment for this state comprises the removal of the person from the stressful situation, and the provision of adequate rest and sleep, and thereafter his prompt return to some useful physical activity.

*Chronic emotional stress* may cause fatigue; it results from prolonged unresolved internal conflict and tension, such as that which occurs in anxiety states and other psychoneuroses. The source of danger lies within the person himself—that is, in the unconscious part of his mind. A person's mind may be likened to a pool of water, the surface of the water representing consciousness. Below the surface lie the various depths of the unconscious part of the mind. Thoughts or ideas that are shameful, undesirable, or disgusting, are repressed; to use a familiar expression, "we put them out of our minds," but actually, we only put them out of the conscious parts of our minds. In the analogy of the pool of water, repressed ideas are like inflated rubber balls that we try to keep submerged. Because of their buoyancy, they constantly seek access to the surface of the water, and we have to use mental energy to hold them down. The effort to suppress unwelcome thoughts, is the source of the fatigue of the psychoneurotic patient. In order to keep these internal conflicts submerged, mental energy is consumed, and exhaustion results. The term "neurasthenia" has been used to describe this type of nervous exhaustion. It was introduced into American psychiatry in 1869 by Beard[3] to whom we should all be grateful, because to say: "I suffer from neurasthenia," sounds so much more dignified than to say "Gee, I'm pooped." According to Masserman,[4] Freud also used the term, which makes it even more acceptable. He considered neurasthenia a symptom resulting from sexual energy that could not be satisfactorily expressed.

The symptoms of neurasthenia are well known, some of which are: lack of energy, fatigability, difficulty in concentrating, ergophobia (fear of work), poor appetite, ennui, and irritability. Physically, the blood pressure is low, the pulse rate is variable, the bowels are irregular, and there may be low back pain, headaches, dizziness, diminished sexual potency.

The "drooping-lily syndrome" is a variant of neurasthenia. An example familiar to all, is that of the social dilettante who arises at noon, consumes several martinis before a modest lunch, is then chauffeur-driven to the beauty parlor, is beautified for an hour or two, is driven home and takes a luxurious nap to recover from the day's exertions. She arises just before dinner and announces to her overworked husband: "My dear, I've had a dreadful day! I'm just *exhausted.*"

Neurasthenia may result from prolonged intense concentrated effort on a project, with resultant tension, irritability, and exhaustion, and an inability to relax after the project has been completed. (Psychiatrists experience this effect at the end of each day of listening to patients and thinking about their problems.)

Vanbrugh,[5] in the seventeenth century, said "Thinking, to me, is the greatest fatigue in the world."

A person who is mentally fatigued may accentuate his fatigue by: irregularity of meals, with consequent lowering of the blood sugar concentration; smoking excessively, with resultant mild carbon monoxide poisoning; having an uninteresting or undemanding job or being bored; getting insufficient sleep; or harboring fear for a prolonged period. Many of these factors pertain to the hard-worked medical resident, and cause what I call "residents' fatigue"—a clinical entity that is well-known, especially among residents.

There is, perhaps, one misconception that may be clarified at this point. It is believed by some that overwork may cause neurasthenic fatigue. I do not believe that overwork causes neurasthenia or leads to nervous breakdown, unless excessive work is utilized as a neurotic defense to prevent unconscious tensions from becoming conscious. One overworked businessman, who finally was hospitalized because his excessive activity led to a state of exhaustion, maintained a busy schedule within the confines of the hospital, and was constantly trying to call his office and continue his business. He finally had to be restrained from such activities. This limitation irritated him, and he became acutely anxious, querying: "But Doc, can't you see that *I've just got to keep working?*"

## Leisure

In considering the treatment of mental fatigue, I want to say a few things about leisure, because the most effective prevention of mental fatigue is the appropriate utilization of leisure.

First let us see how we use leisure and how we relax nowadays. It is my belief that some of our greatest satisfactions are derived from re-enacting experiences that became enjoyable to us early in the course of our development, both physically and culturally. For example, some of us are still on the bottle, although the content is different; the content that we now enjoy is that which makes us less inhibited, less anxious, and more like children—not more like adults. We like to suck objects and to chew things: such as gum, cigars, pipe stems. Some of us like to soak in a hot bath to the accompaniment of soft, rhythmic music. If we were to put out the lights and have food piped in, we would be simulating very closely, the blissful intrauterine existence of the fetus that knows no anxiety, danger, or fatigue. Some of us like to abandon our superb timesaving electric and electronic cooking devices, which in this country are unsurpassed in excellence, and revert to the more primitive technic of throwing onto a pile of hot charcoal a piece of raw meat, the charred remains of which we proceed to devour in some dark corner that is illumined only by smoky, drippy candles. Should we wish to, at the flick of a switch we could have a thousand lumens of light, and tastily

well-cooked meat. And yet, charcoal broiling is a sensible activity. Each one of us has something of the child in him, and it is gratifying to be a child again, to enjoy these developmental and primitive pleasures, and to escape momentarily from the pressures of our adult responsibilities as civilized citizens. "We look before and after; we pine for what is not."*

When a person can relax in the ways described, neurasthenic or mental fatigue is not likely to develop. But if mental fatigue has developed, these suggestions may be helpful. As has been mentioned, mental fatigue results from internal conflict and from tension in situations in which, for one reason or another, appropriate action cannot be taken. Now, appropriate action is not taking a few drinks and then going to bed to try to sleep, for if you are mentally fatigued you probably will not be able to sleep.

Mental fatigue will be alleviated, first by planned diversional activities that are as remote from the person's occupational activities as possible. Thus, physical activity can cause a release of tension and serve as a safety valve. Working off tensions in a gymnasium, on the squash court, or in a swimming pool, or by skating, walking the dog, or in a game of golf, are all recreational activities; they "re-create" the individual by alleviating his tensions.

Secondly, diversional entertainment that provides laughter can similarly relieve mental fatigue. Laughter is an excellent way of relieving tension, and an exhausted person with a good sense of humor has a distinct advantage over the humorless person.

Thirdly, adequate rest is extremely important. Rest enables both body and mind to recuperate in preparation for the stresses of the coming day. We all know how irritable some people are after a 'bad night.' We know they have had a bad night before they tell us. When mental fatigue in the otherwise asymptomatic person interferes with sleep, then I believe that sedation is appropriate therapy.

And perhaps, fourthly, living in a restful and peaceful environment is worthy of mention. It is difficult to relax when there is constant chatter from children, and sound from television, radio, pets, and other sources. It may seem trite to mention, but sometimes it is not easy to obtain a peaceful environment.

## Conclusion

Thus, our minds help us to adjust to the tensions that arise from within and from without, and when fatigue results from unresolved tension we can help ourselves through our effective utilization of leisure.

"What we have not yet learned is . . . how to make our leisure as satisfying, honorable and as creative a part of our lives as work."[6]

*From Percy Bysshe Shelley's "To a Skylark."*

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# INSTRUCTIONS TO THE ILEOSTOMY PATIENT

## Management of the Stoma

RUPERT B. TURNBULL, JR., M.D.

*Department of General Surgery*

EVERY ileostomy patient is instructed in the care of the stoma while he is in the Cleveland Clinic Hospital. The following printed text is given to the ileostomy patient by the enterostomal therapist who personally instructs each patient.

### Instructions to the Patient

To lead a normal life, you must have an appliance that is watertight and comfortable; the fitting must be exact. Although you will be equipped with the appliance before you leave the hospital, you will be asked to see us within three weeks for a final fitting.

There are many types of appliances, but the one most suitable for you at this time will be prescribed. Please do not seek the advice of your friends—either on appliances or on the care of your stoma. Friends mean well, but they do not always know what is best for you. We urge you to consult us personally or by telephone at any time that a problem arises.

The following instructions for the use and care of the ileostomy appliance are presented as a guide for you in the early weeks after operation. If you would like to make changes, for your convenience, you may do so.

### Use and Care of the Ileostomy Appliance

#### Removing the Pouch

Equipment *(Fig. 1)*:

Medicine glass filled with cement solvent
Medicine dropper to apply solvent
Cotton or gauze pledgets

To remove the pouch, you may sit or stand. First, with a ballpoint pen, trace on your skin the outline of the disc. The ink tracing will show you where to apply the cement when you put on the clean pouch. Now push the skin away from the upper edge of the disc, to free it a little, and allow a few drops of solvent to drip from the medicine dropper between the disc and the skin until it loosens the pouch, so that it comes off. *Do not pull the pouch.*

To remove adherent cement from the skin, use cotton saturated with solvent. Wet the skin around the stoma with solvent until the cement is softened. *Do not rub off the skin.* Now wash the skin with water; use a face cloth. A shower or a

*Acknowledgment is made to Mrs. Norma Gill, Enterostomal Therapist at the Cleveland Clinic Hospital.*

bath is good for the skin.

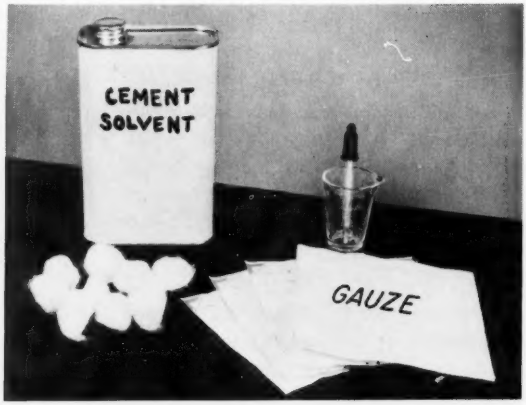



**Fig. 1.** Equipment for removing the pouch.

## Applying the Pouch

Equipment *(Fig. 2)*:

Gum Karaya powder *(Protex powder, Marlen Manufacturing Company, 14807 Kinsman Road, Cleveland, Ohio)*
Talcum powder
Tube of cement in drinking glass
Clean pouch
Paper sleeve
Binder clip (or rubber bands)

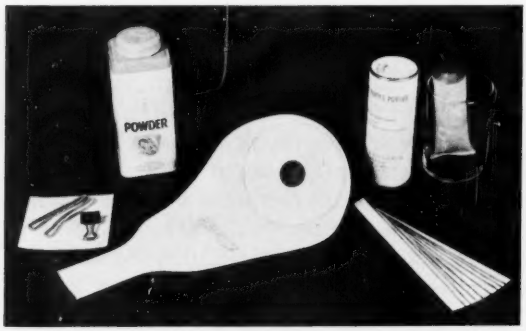



**Fig. 2.** Equipment for applying the pouch.

*Preparation of the skin.* Dust some Protex powder on the red, moist skin immediately around the base of the stoma. After a minute or two blow away the excess powder.

Hold a tube of cement in one hand, and allow a few drops to run onto the index finger of the other hand. Apply these drops of cement on the skin (within the inked circle) around the stoma as near to it as you can with the finger, taking care not to smear mucus from the stoma onto the skin. Spread the cement on one small area at a time, until you have circled the stoma. Apply the cement as thinly as possible.

*Preparation of the pouch.* Lay the pouch down on a flat surface—disc up. Apply one coat of cement to the disc of the pouch as you did on the skin—spread a thin coat of cement on a small area at a time, and *be sure that the cement covers the area near the hole in the disc.*

Repeat the process: apply the cement again to the *skin and to the pouch.*

The cement must be dry and "tacky"—test it with your finger. Now place the paper sleeve in the hole of the pouch until it protrudes ⅛ inch. Using the paper sleeve to "center" the pouch over the stoma *(Fig. 3, A, B, C),* apply the pouch firmly to the skin.

Press the disc of the pouch tightly to the skin for a few minutes until it is cemented firmly in place. The paper strip will fall into the pouch.

Dust talcum powder on the skin around the disc.

## Cleaning the Appliance

Equipment:

Basin of water
Liquid detergent, *Handy Andy, Mr. Clean, Pine-sol, Lestoil,* or *Clorox*
*Chlorazene* tablets (Marlen Manufacturing Co.)
Drying hanger (from pouch manufacturer)
Talcum powder
Cement solvent
Nylon brush (Marlen Manufacturing Co.)

The pouch should be removed and should be cleaned daily. You may use one or a combination of liquid detergents, and cleaning agents such as *Handy Andy, Mr. Clean, Pine-sol,* or *Lestoil,* in water. A small amount of *Clorox* may be added.

With a piece of cotton saturated with solvent, remove the cement from the disc and pouch. Place the pouch in a basin of water to which detergent has been added; to deodorize the pouch you may also add *Chlorazene* tablets (Marlen Manufacturing Co.) to the water. Scrub the inside of the pouch with the long nylon brush (Marlen Manufacturing Co.) and soak the pouch for 10 minutes; rinse it with clear water; and hang it up to dry on a drying hanger. Dust the dry

pouch inside and outside with talcum powder to prevent sticking of surfaces.

Soak the pouch for an hour or more, once a week, in water with detergent and *Chlorazene* tablets.

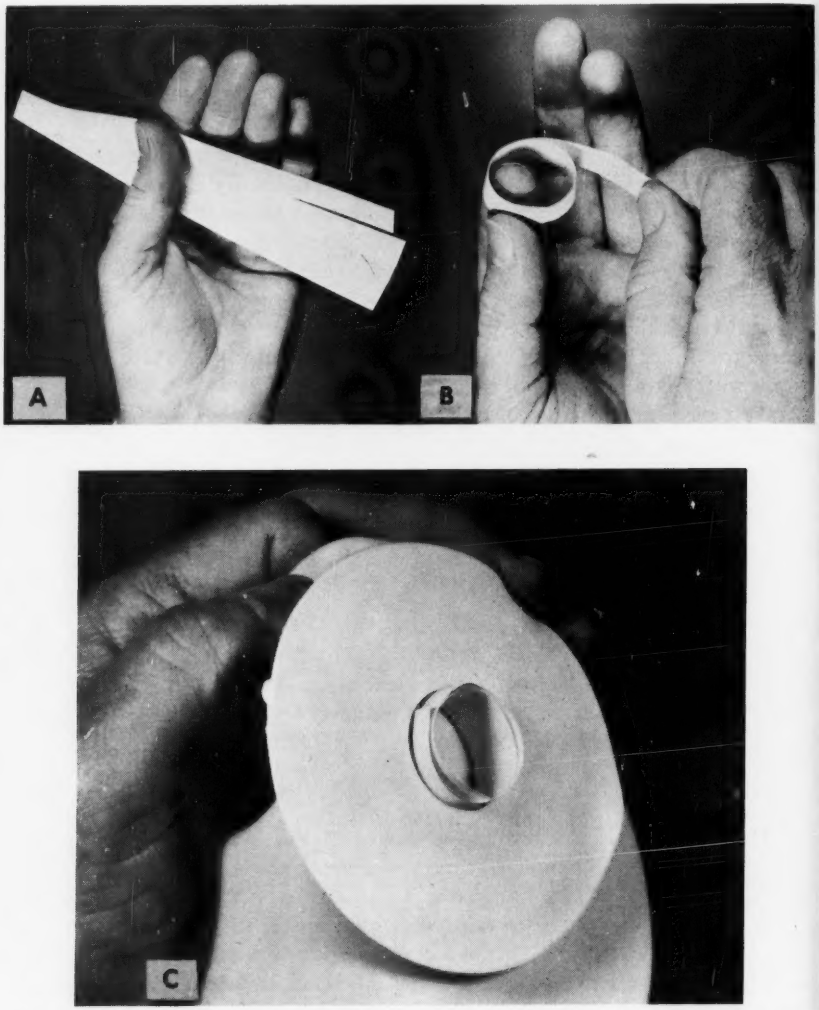



**Fig. 3.** Use of the paper sleeve for centering the pouch. A, Narrow strips of bond paper. B, Coiling a strip to fit the aperture of the pouch. C, Paper sleeve in place. (Courtesy of: R. B. Turnbull, Jr., M.D., Ileostomy Quarterly, Spring, 1960.)

### Emptying the Pouch

The pouch should be emptied every two or three hours, depending on how fast it fills. Do not let it fill up and "blow off" at night. You can prevent this from happening if you limit the amount of food and fluid you take just before bedtime; or you may wish to wear a large pouch at night. Do not lie on the pouch when it is full or partly full.

### Accidental Detachment of the Pouch

If the pouch should accidentally come off, you did not apply it correctly. Repeat the entire process of applying the pouch, paying particular attention to *spreading of the cement accurately on the skin and on the disc of the pouch.*

### Ordering the Appliance and Supplies

Your pouches were purchased for you from one of several companies. The manufacturer keeps a record of your size and all other details necessary to know when you reorder from him.

Write to the manufacturer direct for cement, cement solvent, extra pouches, and belts.

Binder clips (or rubber bands), to close the end of the appliance, are available at any stationery store. Take one of your old clips with you when you go to purchase new ones.

When ordering supplies, allow 10 days for delivery.

## Discussion

The stoma represents the end of the small intestine brought to the skin. (The large intestine or colon has been removed.) Digestion is completed in the small intestine, and by the time most foods reach the stoma they are in the form of a brown, green, or yellow liquid that has little odor.

For the first several weeks after the operation, the stoma is a little stiff and noisy, and it may cause cramps. There is a slight egglike odor. The stiffness, noise, gas, and cramps are caused by swelling, but the swelling soon subsides. After a few weeks, there is no odor or noise or cramps.

### Special Problems—Swelling of the Stoma, Cramps, and Watery Diarrhea

You can damage the stoma with the appliance if it is not centered properly, or if it "slides" against the stoma. This damage is in the form of a cut on the *undersurface* of the stoma. When the stoma swells and runs excessively, turn it upward and look at it carefully with a hand mirror. You will see a cut near the skin that will bleed and may be painful when it is touched *(Fig. 4).* Such a cut can cause swelling, cramps, odor, an excess of gas, and noise. Should this occur,

**Fig. 4.** Photo of the cut undersurface of the stoma.

put on the first application that you received when you were discharged from the hospital (it has a large opening); or cement on a Marlen postoperative pouch.

Should the cramps become unbearable, irrigate *(Fig. 5)* the stoma by repeatedly injecting salt water (one heaping teaspoonful of salt to one quart of warm tap water). Inject the water through the snout of the baby's ear-syringe, or a special tube you received when you were discharged from the hospital. You may have to irrigate every hour, for two or three hours, to remove food particles completely.

### Obstruction of the Stoma

The stoma is the narrowest part of the small bowel, and it may become "stopped up" (obstructed). Obstruction results from cutting the undersurface of the stoma (with consequent swelling as described under the heading, **Swelling of the Stoma, Cramps, and Watery Diarrhea**) or, more often, from eating large amounts of food that are listed as undesirable. (See ILEOSTOMY DIET.) Since these foods do not digest completely, they are conveyed down the small intestine to a point just inside the stoma where they accumulate and form a "dam." Irrigating the stoma (as described under the heading **Swelling of the Stoma, Cramps, and Watery Diarrhea**), will dislodge clumps of residue and will allow them to pass. Unrelieved obstruction of the stoma can become a serious matter and may lead to vomiting. If this happens, you should contact your doctor or a member of his staff by telephone.

### Skin Care

Should any portion of the skin to which the pouch is cemented become irritated and present a red wet surface, dust Protex powder on it and blow away

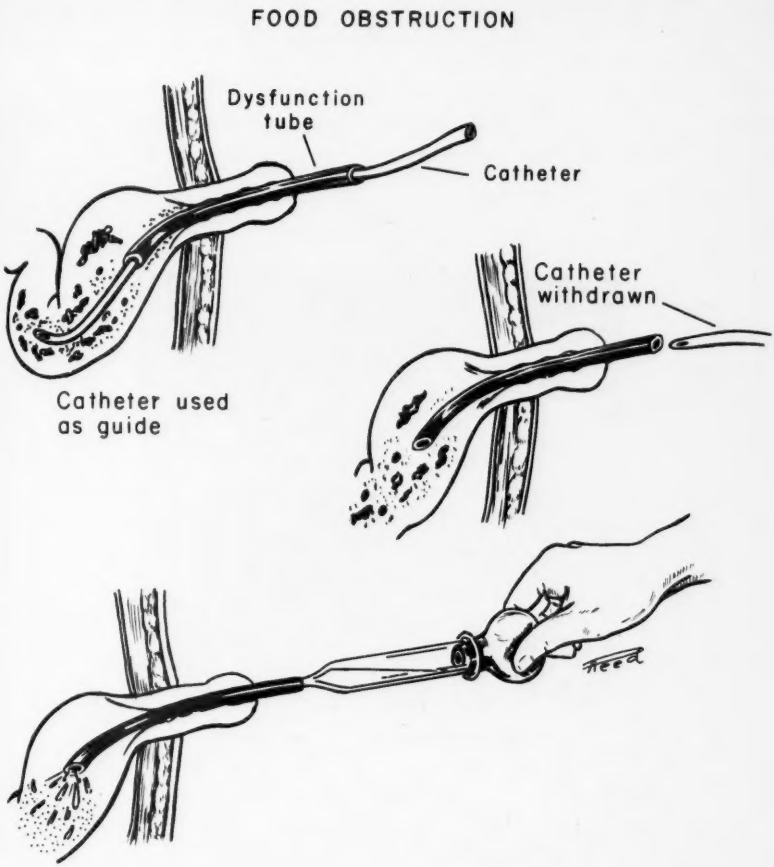



**Fig. 5.** Irrigation through the stoma.

the residue. The cement can then be applied right over the powdered areas. Remember that this gumlike powder sticks to the cementing surface of the appliance, and must be scrubbed off before more cement is applied later.

Persistent skin blemishes, shallow ulcers, or red wet areas may appear near the stoma. These are caused by pulling the disc off instead of allowing the solvent to dissolve it off. These shallow ulcerated areas may spread and may burrow rapidly under the skin in a few days. This progression can be prevented as follows: after the pouch is removed, dissolve the cement from the skin. Take a long soaking bath or shower; dry the skin, then apply cement, but avoid touching each blemish

or ulcer. Cut bits of folded gauze *(Fig. 6)* to the size of each ulcer and cover each one individually. Now, apply the pouch. Repeat this morning and night until the areas are healed.

Remember that solvents should be removed from the skin with a wet cloth before applying cement. They are irritating. Always allow the cement to dry before applying the pouch. "Wet" cement may blister your skin.

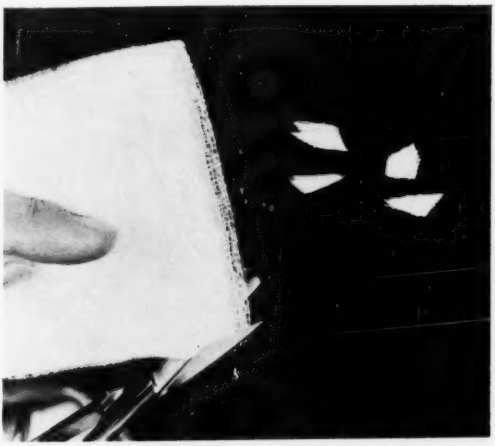


**Fig. 6.** Gauze bits to cover skin ulcers.

## Diet List

A diet list is presented on the last pages of this booklet. It itemizes the foods that you are allowed and those that you are not allowed to eat. We ask you to follow this diet carefully for at least six weeks; but thereafter, you may eat moderate amounts of the foods listed as undersirable. Large portions can cause obstruction. Remember that *cole slaw, popcorn, canned fruit salad, nuts,* and *shrimp* are never entirely safe to eat.

## Baths and Showers

Baths and showers may be safely taken at any time. When the stoma is active, and you wish to bathe, wear the appliance in the tub, but change it after you come out. We suggest that you remove your appliance and then shower or bathe to take advantage of the favorable effect of water on the skin around the stoma. Remember: water and soap will not harm the stoma in any way.

## Sports

You may participate in most sports. For swimming and other sports you may wish to add adhesive tape over the edge of the disc to provide an extra seal. Wear a tight undergarment to hold the pouch to your abdomen.

## Manufacturers' Names and Addresses

Marlen Manufacturing Co.
14807 Kinsman Road
Cleveland, Ohio

Permatype Inc.
1559 New Britain Avenue
West Hartford 10, Connecticut

Torbot Company
170 Vine Avenue
Warwick, Rhode Island

## Appliances

Appliances that we most frequently use are illustrated on the next four pages *(Figs. 7, 8 A and B, and 9 A and B).*

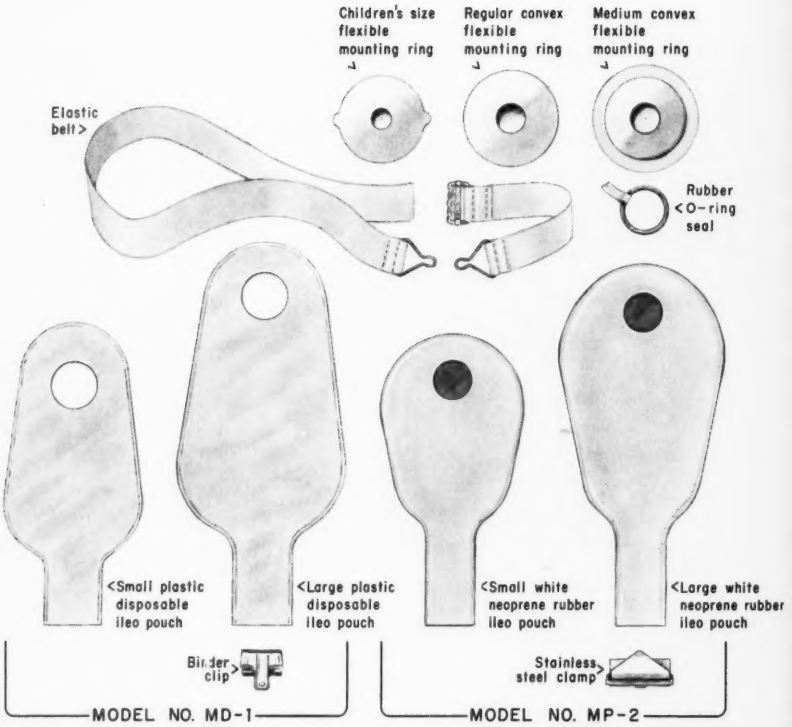



Fig. 7. Marlen Manufacturing Company appliances.

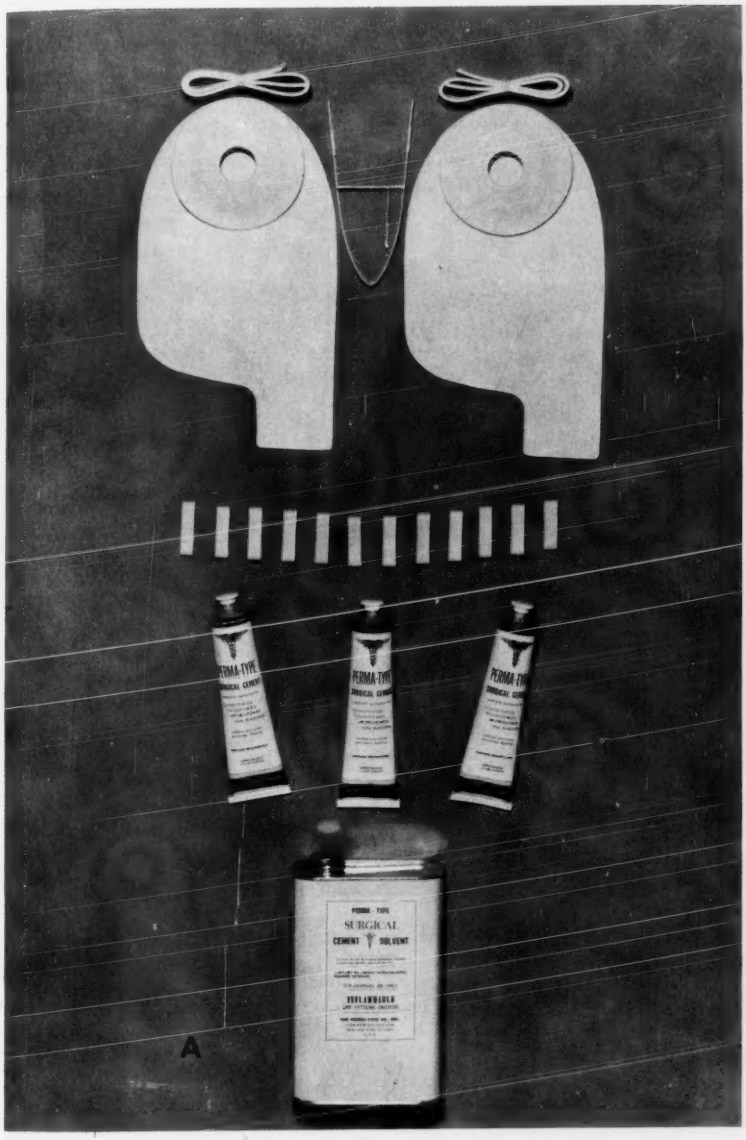



Fig. 8. Perma-Type Co., Inc.: A, Appliances.

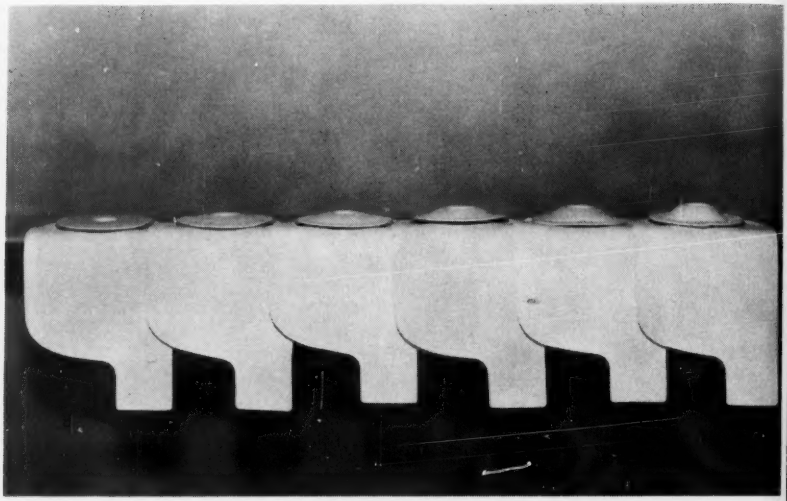
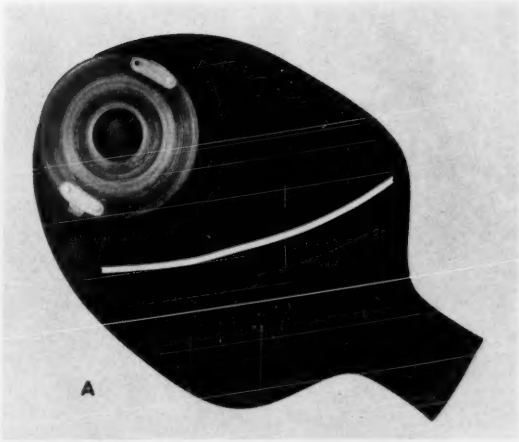


**Fig. 8.** Pouches showing discs of various convexities available.



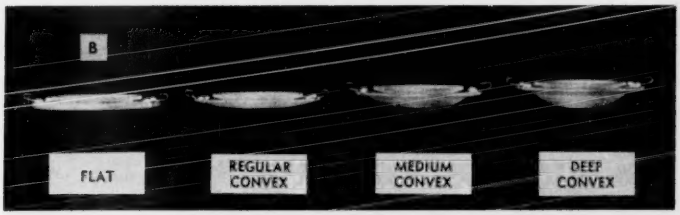




Fig. 9. Torbot Company: A, Pouch with plastic disc; B, various convexities of plastic discs available.

## CLEVELAND CLINIC ILEOSTOMY DIET

| Foods Included: | Foods Excluded: |
|---|---|
| **Fruits**<br>*Strained:* stewed prunes, applesauce, apricots, peaches, white cherries, pears. Any strained fruit juice. | *Raw* whole fruits. Cooked fruits or canned fruits. *Dried* fruits such as raisins, dates, figs. |
| **Cereals**<br>Cream of Wheat, farina, Wheatena, rice, barley, strained oatmeal, corn-flakes, Corn Kix, Puffed Wheat, Puffed Rice, Wheaties, Shredded Wheat, Muffets. | Those containing bran such as All Bran, 40% Bran Flakes. |
| **Breads, etc.**<br>White, refined whole wheat, graham, or rye (no seeds); simple wafers or crackers. Arrowroot crackers, Melba toast, Zwieback, Holland Rusk, rolls, muffins, baking powder biscuits, waffles, pancakes. | Cracked-wheat bread; muffins or rolls made with bran; muffins or rolls made with whole fruit such as blueberry muffiins. Bread, rolls or muffins made with nuts, dried fruits such as raisins, or seeds such as poppyseeds or caraway seeds. |
| **Eggs**<br>Soft boiled or hard boiled, poached, scrambled, omelet, fried, creamed, or as soufflé. | |
| **Soups**<br>Cream soups made with rice, potato, or with allowed vegetables. Clear broth or broth with noodles or rice. Strained broth from soups made with whole vegetables such as mushrooms. | Soups containing whole vegetables such as corn chowder, pepper pot, or mixed vegetables. |
| **Meats and Fish**<br>Beef, lamb, veal, pork, bacon, ham, liver, sweetbreads, domestic rabbit, loose sausage, luncheon meats, chicken, turkey, squab, duck, goose, oysters. Fresh, smoked, or canned fish. Meats may be broiled, boiled, roasted, or fried. | Meats in casings. Luncheon meats with peppercorns, pimento, or other whole spices.<br>Lobster, shrimp, crab, and fish may cause odor or obstruction. |

## CLEVELAND CLINIC ILEOSTOMY DIET—*concluded*

| Foods Included: | Foods Excluded: |
|---|---|
| **Potatoes, etc.**<br>White potatoes — baked, mashed, boiled, creamed, or escalloped. Sweet potatoes, spaghetti, rice, noodles, macaroni, or hominy. | Potato skins, potato chips, fried potatoes. Spaghetti sauce that contains whole vegetables such as mushrooms or green peppers. Wild rice or brown rice. |
| **Vegetables**<br>Strained—peas, beets, string beans, wax beans, carrots, asparagus, spinach, finely shredded crisp lettuce. (Baby-food vegetables may be used to save straining vegetables at home.) Any vegetable juice. | Whole vegetables. |
| **Desserts**<br>Custards; puddings such as cornstarch, rice, tapioca, and bread. Cakes such as angel food, sponge, chocolate, plain white cake; cookies. Ice cream, sherbets, gelatin desserts, fruit whips. Pastries such as cream puffs; pies such as custard, pumpkin. | Any desserts containing excluded fruits, nuts, or coconut, such as fruit cake. Pineapple sherbet, coconut cookies. Pies made with whole fruit such as berries, raisins, or mincemeat. |
| **Beverages**<br>Coffee, tea, Sanka, Kaffee Hag, Postum, carbonated beverages. | |
| **Miscellaneous**<br>Cheese may be used as desired if tolerated. Any fats such as butter, margarine, oils, salad dressings, and cooking fat. Smooth peanut butter. Pretzels. All seasonings and condiments such as mustard and catsup. Candies, jellies, honey, syrups, and molasses. Gravies, whitesauce, and vinegar. | *Milk* in any form if it causes diarrhea or if it has not been tolerated in the past.<br>Garlic. Chili sauce with seeds. Popcorn. Relishes made with whole vegetables such as piccalilli, or pepperhash. Nuts, jams, marmalades. Pickles and olives. |

## SAMPLE MENU

### *Breakfast:*

**FRUIT**
. . . Strained orange juice
**CEREAL**
. . . Cream of Wheat
**EGG**
. . . Poached egg with bacon
**BREAD**
. . . Toast with butter and jelly
**BEVERAGE**
. . . Coffee with cream and sugar

### *Lunch:*

**SOUP**
. . . Chicken rice soup
**MEAT OR SUBSTITUTE**
. . . Cheese soufflé
**POTATO**
. . . Baked potato
**VEGETABLE**
. . . Strained carrots
**BREAD**
. . . Whole-wheat bread and butter
**DESSERT**
. . . Strained apricots
**BEVERAGE**
. . . Milk, tea, or coffee, as desired

### *Dinner:*

**SOUP**
. . . Broth
**MEAT**
. . . Roast beef with gravy
**POTATO**
. . . Mashed potatoes
**VEGETABLE**
. . . Strained peas
**BREAD**
. . . White bread with butter
**DESSERT**
. . . Ice cream
**BEVERAGE**
. . . As desired

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[1] *Formerly Special Fellow; present address: Charles Camsell Indian Hospital, 114th Avenue and 128th Street, Edmonton, Alberta, Canada.*

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